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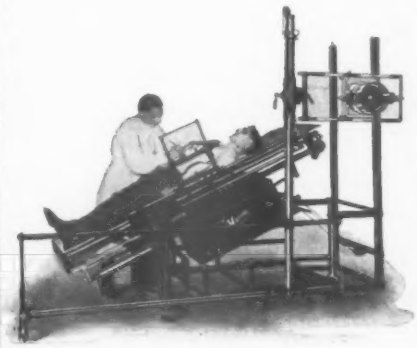

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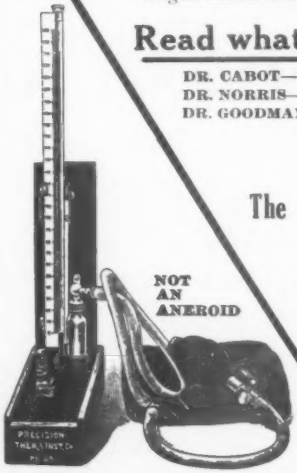


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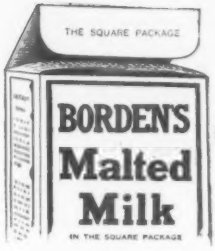


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SEPTEMBER, 1917

## ORIGINAL ARTICLES

### A CASE OF ADAMANTINOMA SHOWING EPITHELIAL PEARLS.

By Stuart Graves, M.D.,
Louisville, Kentucky.

(From the Pathological Laboratory of the Medical Department of the University of Louisville and of the Louisville City Hospital.)

Tumors arising from embryonic structures of the teeth are comparatively rare. The majority of such neoplasms are reported as "odontomata." According to Mallory,[1] three types of tumors of the jaw are recognized as arising from embryonic remains of the enamel organ. These are:

1. The follicular cyst, which is the simplest. It consists of a cyst lined with pavement epithelium. The inner wall of the cyst often bears a single, rarely several to many teeth.

2. The adamantinoma, growing as branching masses of epithelial cells, of which those adjoining the stroma correspond to adamantoblasts while the others form the enamel pulp. Cysts often form, owing to distention and coalescence of the vacuoles lying between the cells corresponding to those in the enamel pulp. Other cysts, which may be more numerous and larger, often occur in the connective tissue of the stroma as the result of focal collections of fluid. Blood-vessels will always be found running through this second form of cyst. Rarely the cells corresponding to those in the enamel pulp assume a concentric arrangement or may even form definite epithelial pearls. This result is not surprising, considering the origin of the enamel organ. The adamantinoma grows expansively only and

[1] Principles of Pathological Histology, second edition, p. 285.

does not produce metastases. Owing to its location and the size it sometimes reaches it may cause clinically much local disturbance.

3. The odontoma, which is produced by the conversion of fibroblasts adjoining the adamantoblasts into odontoblasts as a result of the action of the adamantoblasts upon the fibroblasts. When this happens separate teeth or fused masses of them may be produced by the differentiation of the odontoblasts with the adamantoblasts. Cementum may sometimes be formed. Occasionally the adamantinoma produces typical enamel.

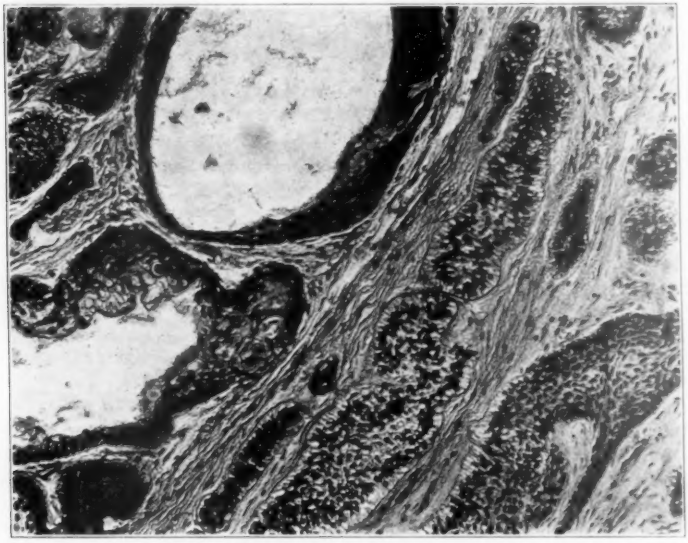

FIG. 1.—Adamantinoma. Cysts forming between pulp cells. Multiplied 150.

Adamantoblastoma, then, is a generic term like fibroblastoma, and covers the adamantinoma, developing from epiblastic cells which normally differentiate into adult enamel, and the odontoma, including not only the tumor structures of the adamantinoma, but also those structures arising from mesoblastic odontoblasts which normally differentiate into dental pulp, dentine, and cement. The structures of the adamantinoma are included in the odontoma because the structures of the latter are stimulated to growth by the action of the adamantoblasts upon the mesoblastic stroma, just as proliferative activity on the part of fibroblasts is incited by other tumor cells. The odontoma is a more highly differentiated type of adamantoblastoma just as a dermoid cyst is a more highly differentiated form of embryoblastoma than is a rapidly growing embryoma,

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more commonly called a round or spindle-cell sarcoma or a carcinoma.

The adamantoblasts normally begin as an invagination of the oral epithelium and develop into the enamel organ covering the mesenchymal dental papilla. The enamel organ consists of an outer layer of enamel cells lying next to the surrounding gum and an inner layer of enamel cells lying next to the dental papilla. Between the two layers is the enamel pulp, consisting of epithelial cells corresponding to the prickle cells of the epidermis. "At first these internal cells are in close contact, like those of ordinary epithelium; but later, through vacuolization and accumulation of gelatinous, intercellular substance, they constitute a protoplasmic reticulum which resembles mesenchyma, and is known as the enamel pulp."[2] An excessive accumulation of this secretion, with abnormal coalescence and distention of the spaces, gives rise in tumors to cysts filled

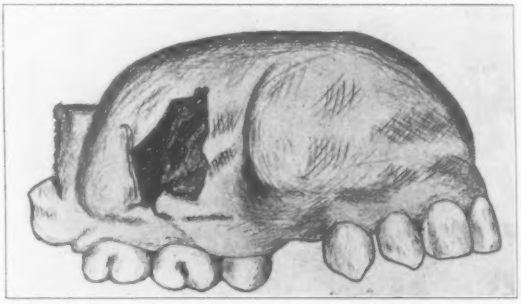

FIG. 2.—Adamantinoma reproduced with pen and ink from Kaiserling preservation of lateral half of specimen and from written description. (McCrocklin.)

with gelatinous, sticky, semifluid material. Larger cysts are also formed in the stroma of such tumors by the accumulation of fluid, and are surrounded with cylindrical cells whose nuclei are away from the stroma, and hence from the cysts. These two kinds of cysts are characteristic of the cystic adamantoblastomas. In the normal embryonic enamel pulp no vessels or nerves are found, but in the stroma of neoplastic growths arising from remains of the enamel organ, vessels do occur as they do in the stroma of all tumors. The larger cysts form about these vessels.

In the process of invagination and development of the enamel organ the inner enamel cells (ameloblasts) elongate and become the enamel-producing cells (adamantoblasts). According to Lewis and Stohr[3] "the ameloblasts produce enamel along their basal surfaces, which are toward the dental papilla; but they become so trans-

[2] Lewis and Stohr: A Text-book of Histology, second edition, p. 102.
[3] Loc. cit.

formed that their basal surfaces appear like free surfaces and the entire cells seem inverted. In columnar epithelial cells the nuclei are generally basal and the secretion gathers near the free surface, but in the ameloblasts these conditions are reversed. The nuclei are toward the enamel pulp and the latter forms a dense layer over the ameloblasts," while what were the basal ends of the cells before invagination, which now lie next to the dental papilla, appear free and without nuclei. In the microscopic picture of adamantoblastoma most of the cysts are in the stroma, as a rule, and are lined with the apparent free ends of the cylindrical epithelium whose nuclei are in the opposite ends away from the cysts. In other words, the

FIG. 3.—Adamantinoma, from photograph of Kaiserling. Preservation of lateral half of specimen.

ends which were basal before invagination and contained the nuclei are now free and adjacent to the cysts in the stroma. This is another characteristic picture of adamantoblastoma.

In connection with the case herein reported it is interesting to note that it occurred in a negro child. Miller,[4] in presenting clinically a case of unilateral odontoma of the superior maxilla in a two-year-old colored child, diagnosed with the aid of skiagrams which showed numerous widely scattered teeth, says: "Slowly growing unilateral jaw tumors are not infrequent in colored people and often attain huge size. These are commonly odontomata or

[4] Philadelphia Acad. Surg., 1914, xvi, 35.

adamantine in character." Westmoreland,[5] in presenting a tumor which he called a "follicular odontoma" in Bland-Sutton's classification, made the observation that these tumors seemed to be disappearing, he not having seen a case for years, although he had operated on 5 cases and his father on 38, all save one in negroes.

This report is submitted because it is that of an adamantinoma developing purely from adamantoblasts, shows epithelial pearls, and occurred in a sixteen-year-old negro boy. The specimen was removed by Dr. H. H. Grant from the superior maxilla on March 1, 1916, in the Louisville City Hospital and was sent to the laboratory with a clinical diagnosis of osteosarcoma. The tumor had been first

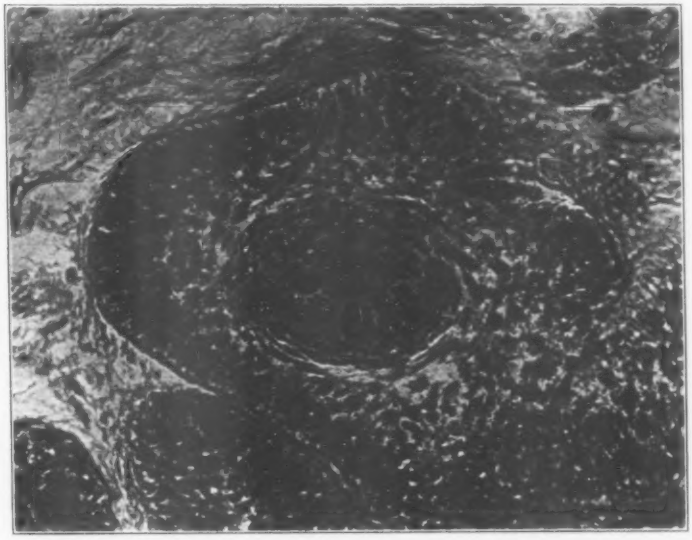

FIG. 4.—Adamantinoma, showing epithelial pearls. Multiplied 400.

noticed about one year before as a swelling of the gum, had grown gradually and been painless. The gross description of the specimen is as follows:

GROSS DESCRIPTION. Specimen consists of a portion of right superior maxilla with tumor. Three incisors, one canine, two molars, and adjacent bicuspid are present in their normal positions. Shaft of bone is severed transversely 1 cm. outside of lateral molar. Its superior surface is smooth and covered with muscle. Medial end is 2 cm. at left of cleft, between middle incisors. Anterosuperior surface bears a rounded mass covering practically all the surface.

[5] Westmoreland: Surg., Gynec. and Obst., 1911, xii, 188.

Mass presents a cavity extending from upper to lower margins of specimen, 25 mm. wide and 15 mm. deep anteroposteriorly. This cavity is covered in front with a firm, cartilaginous shell, 1 to 3 mm. thick, and opens anteriorly in lower portion through an orifice 15 x 25 mm. Inner surface of cavity is smooth and does not present any teeth. Greater portion of remainder is smooth, moderately firm, and covered with a fibrous capsule bearing tags of muscle in upper portion, and presents a transverse, ragged crevice, apparently artificial. Tumor mass extends around underneath gum between canine and lateral bicuspid. In this space it is smooth, pale, and moderately firm. On sagittal section, through middle of mass, cut surface presents inferiorly, hard, cancellous bone 7 mm. thick, which extends upward about two-thirds of circumference of posterior surface. Anterosuperiorly tumor is bounded by a very thin, pale, white shell. Between these limits the tissue varies from white and pale gray, firm tissue to soft, pink and pale creamy brown tissue. Scattered in cut surface are small, irregular, pale spots cartilaginous to bony in consistency. On sagittal section through bicuspid there is opened anteriorly a smooth-walled cyst, unilocular, bounded by a thin, pale membrane, and containing pale brown fluid material distinctly gelatinous. It sticks to fingers like secretion from thyroid. This cyst is 15 mm. in greatest diameter and its bottom is 12 mm. above root of bicuspid. A smaller, similar cyst lies peripherally at superoposterior border of the specimen. Another sagittal section medial to first shows cut surface circumscribed as others, but solid and varying from pale gray to straw color and from bony hardness to soft. From surface of this is given off considerably more stringy, gelatinous material. After fixation numerous small holes are seen in cut surface. Sagittal section of one tooth in normal position shows root imbedded in maxilla at base of tumor mass. Sections of one-half of the specimen do not reveal any signs of teeth within the tumor.

Microscopic Description. Ten sections through different parts of the tumor show more or less similar structures; small to fairly large, irregular, sharply outlined, branching masses of compact cells. The grouping of the tumor cells suggests the arrangement of the compact epithelial cells in a hair matrix carcinoma. These are supported by a fibroblastic stroma in which is seen an occasional small vessel. The tumor cells are round to spindle in shape, have very little cytoplasm and contain small, fairly deeply staining nuclei. The cells about the peripheries are high columnar in type and have oval nuclei in the ends away from the stroma. Many of the tumor cell groups near their centers exhibit cells with vacuolization and small to moderately large cavities in which is a finely beaded material which stains homogeneously with eosin-like fine droplets of colloid. Some cells are in concentric layers like epithelial pearls. Some of these cavities are large and surrounded only with a rim

of tumor cells which are cuboidal rather than columnar at the periphery. Some of the sections show particles of bone in the stroma. Section from the block cut sagittally through a tooth shows a normal tooth outside the tumor.

MICROSCOPIC DIAGNOSIS. Adamantinoma.

In conclusion, I wish to express thanks to Professor F. B. Mallory for critically reviewing this article and the sections; to Mr. L. S. Brown, of the Massachusetts General Hospital Laboratory for his kindness in making the photomicrographs, and to Mr. Walter McCrocklin, a student in our laboratory, for the sketch drawn from the museum preparation of half the gross specimen and from the description in the laboratory records.

NOTE.—Since this article was written the boy reported five months after operation and showed no sign of recurrence.

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## THE PATHOLOGICAL AND CLINICAL ASPECTS OF THROMBO-ANGIITIS OBLITERANS.[1]

BY LEO BUERGER, M.D.,
NEW YORK.

IT is not my purpose to burden you with an extensive and detailed account of the pathological and clinical aspects of the disease thrombo-angiitis obliterans, because the clinical picture and the main facts regarding the pathological lesions are certainly sufficiently known to you. I shall attempt, rather, to present the subject matter from the view-point of one who has been fortunate enough to have had a large amount of clinical material at his disposal (more than 300 cases), from which all phases of the pathology and clinical course could be investigated.

Perhaps the best general view of the morbid process, the most thorough understanding and most satisfactory conception can be had by a general comparative consideration of the pathological lesions and their corresponding clinical manifestations.

If I were asked to formulate a general concept of thrombo-angiitis obliterans I should answer as follows: Imagine a patient seeking relief for acutely swollen superficial veins of the lower or upper extremities, of sudden advent, and with all the manifestations of an acute thrombophlebitis. Imagine this process involving a considerable portion of the distal territory of the internal saphenous vein, followed by abatement of symptoms, and consequent resolution or healing. You will be in no doubt as to the general pathology nor as to the clinical course of the condition,

[1] Read before the College of Physicians of Philadelphia.

though your estimation of the etiology will in most instances, at least, be obscure.

Transfer this picture to the deeper vascular system, over the distribution of the external and internal plantar arteries and veins, the dorsalis pedis, anterior tibial, posterior tibial, and the peroneal arteries and veins, that is, with lesions in territories where objective manifestations are absent—and you will be depicting to yourselves, what corresponds to my own conception of the pathological process in the disease, thrombo-angiitis obliterans. So here, too, we postulate an acute inflammatory and thrombotic lesion, but one involving deep arteries or veins, or both, as the initial stage of the pathological anatomy.

Whereas the patient afflicted with an inflammatory and thrombotic lesion of the superficial veins presents objective signs easy of recognition, the patient suffering from thrombo-angiitis obliterans in its earlier stages may offer no objective evidences suggestive of the true nature, or of the site of the lesion. It was but in a very few cases of my own series (more than 300) that I felt justified in ascribing certain symptoms to the incipient stage of the disease. Severe, non-localizable shooting pains in the calf or foot, attended with difficulty in walking, or, possibly, with tender calf muscles, with or without vasomotor symptoms and coldness in the foot, with or without obliteration of the dorsalis pedis and posterior tibial pulses, may be the only symptoms. It is only when we compare the history with the future clinical course and pathology that we can relegate such indefinite signs to the onset of the affection. In most instances, however, the patient will not seek advice for such initial symptoms, either because they are not sufficiently severe to require the attention of a physician, or because they are incorrectly regarded as rheumatic in origin, possibly due to trauma, cold, the presence of flat or weak foot, or because they are explained on the basis of some other minor ailment.

Strange to say, patients afflicted with thrombo-angiitis obliterans may present symptoms which differ in no way from those attending the thrombophlebitis of the superficial veins, or so-called migrating phlebitis. These are the cases of thrombo-angiitis obliterans in which an acute inflammatory thrombosis involves smaller or larger portions of the external or internal saphenous vein, radial, ulnar, median cephalic or median basilic vein. Such cases are the most instructive of all, for they are the ones which afford us material for pathological study. Here the veins are accessible; portions can be surgically removed when the lesions are in the acute inflammatory stage and submitted to histological examination.

While the former type of case is difficult to diagnose the variety with concomitant migrating phlebitis can be recognized by a

study of the vein lesions under the microscope. If the tissue be examined when the lesions are still in the early inflammatory stage, before organization or healing has taken place, certain characteristic and specific lesions can be identified, changes which I have elsewhere described as pathognomonic for thrombo-angiitis obliterans.

Having learned that the incipient lesion of thrombo-angiitis obliterans is an acute inflammatory one, involving the arterial and venous walls, we will expect an occlusive thrombosis as the immediate sequence, and will not be surprised to learn that this stage gradually gives way to one of organization and canalization, resulting in a healed product in which the vessel becomes converted into a cord, more or less adherent to its surroundings, in which even the neighboring nerves may become agglutinated and enveloped in fibrotic vascular cord.

It is the interference with the circulatory conditions of the limbs brought about by the extensive occlusive process that is responsible for most of the clinical manifestations of thrombo-angiitis obliterans. So that it may be safely said that patients afflicted with thrombo-angiitis obliterans do not suffer directly from the disease itself but from the disastrous occlusive thrombosis which signalizes Nature's method of healing a vascular lesion, that has long since disappeared.

From a study of the pathological material, and from a comparison of the lesion with the clinical history, we must conclude that insidious or clinically unrecognizable exacerbations of the lesion may occur from time to time, so that the involvement of the vascular territory with the obliterative lesion is a progressive one until the summit of the organized clot reaches the popliteal, in rare cases the femoral or even the iliac. It will not occasion astonishment, therefore, that the clinical manifestations, too, become more and more serious as time goes on.

Nor must we be surprised if thrombo-angiitis obliterans simulates clinical complexes brought about by arterial occlusion from other causes. Differentiation from arteriosclerotic gangrene, intermittent claudication due to arteriosclerosis, endarteritic occlusion, and other thrombotic conditions may at times be difficult. It is the fact that thrombo-angiitis obliterans occurs in *very young individuals* in whom both the *vis a tergo* and the cardiac power are adequate for compensation, and in whom the vascular adaptability is elastic in its scope—it is this fact that accounts for the seemingly almost inexplicable circumstance, that gangrene occurs *so* late, or may be absent, in spite of vast and extensive obliteration of arteries and veins. It is to the development of the collateral circulation, therefore, that we owe, in part at least, the production of a very peculiar, striking, and characteristic clinical picture, recognizable even though mani-

festations of the acute stage of the disease, or manifestations, such as migrating phlebitis, are absent.

Clinical Symptoms. I will not go into detail concerning the clinical symptoms, for they are sufficiently well known. It may be interesting merely to make brief mention of my own routine method of physical examination, one that has stood me in good stead, in the recognition and also in the differentiation of this disease from those other that closely simulate it, and then to illustrate by lantern slides the chief feature of the pathology of the disease.[2]

My own scheme includes the investigation of the following points: (1) the general appearance of the limb in the horizontal position; (2) in the pendent position; (3) the presence or absence of ischemia in the elevated position; (4) the estimation of the *angle of circulatory sufficiency*; (5) pulsation in the palpable vessels, iliac, femoral, popliteal, posterior tibial, anterior tibial, and dorsalis pedis in the case of the lower extremities, radial, ulnar, brachial, and axillary in the upper extremities; (6) the occurrence of *induced, reactionary rubor* or *erythromelia*.

1. The General Appearance of the Limb. Any departure from the normal should be noticed. The presence of fissures, ulcers, perforating ulcers, bullæ, ecchymoses, impaired nail growth, gangrenous areas, signs of infection or lymphangitis or venous thrombosis, evidences of malnutrition, such as atrophy, exceptional prominence of the bony landmarks and extensor tendons, conservation or effacement of the normal irregularities of contour through edema or through thickening of the skin and subcutaneous tissues, are features of importance. Variations from the normal color—particularly marked pallor in the horizontal position, a play of color over the foot, even in the horizontal position; cyanosis, increased redness—all these are manifestations of either impaired circulation or vasomotor disturbance.

2. In the Pendent Position. With the foot in the pendent position and in the absence of inflammation a red flush involving the toes and dorsum, as well as the sole of the foot, extending upward for a variable distance, rarely farther than the ankle, is a phenomenon that is characteristic of many cases and many types of reduced circulation due to vascular obturation. This is a condition of *rubor* or *erythromelia* (Gr. *erythros* = red, *melia* = limb). It is brought about by a compensatory dilatation of the superficial capillaries, and is most characteristic of the disease, thrombo-angiitis obliterans, although also found in other arterial affections attended with closure of larger vessels. It is frequently present in

[2] The lantern slides are not reproduced in this paper; some have been published in previous papers on thrombo-angiitis obliterans.

arteriosclerotic and diabetic cases as well. It seems to be an effort on the part of Nature to make up for the impairment of circulation by virtue of dilatation and engorgement of the superficial capillaries. Although more striking in the pendent position the rubor may also be present in the horizontal position, and when continuously in evidence may be termed *chronic rubor* and *chronic erythromelia* in contradistinction to the *reactionary rubor* that may be induced by depressing the limb after previous elevation.

3. Ischemia or Blanching. This usually sets in rapidly when the affected limb is elevated whenever mechanical interference with the circulation is present. The extent of blanching and the rapidity with which it appears are both valuable aids in the estimation of the amount of obstructive arterial disease. When the affected limb is cold the tips of the toes may remain slightly blue or cyanotic. Should the blanching be slow in appearing, or very hard to determine, pressure upon the tips of the toes after the limb has been elevated for some time will demonstrate whether the part has become depleted of blood or not ("expression test"). Compression of the toes of the elevated foot in normal cases will reveal the presence of sufficient bright arterial blood (rarely slightly cyanotic), while a varying degree of ischemia, with or without marked cyanosis, will accompany obliterated or obstructed arteries.

4. The Angle of Circulatory Sufficiency. The estimation of this angle is based on the supposition that the normal limb, when elevated so as to be perpendicular to the horizontal plane, that is 180 degrees, still retains most of its color. When the circulatory mechanism is defective, and the limb is elevated to the vertical, a variable degree of blanching of the foot occurs. If the leg is then gradually depressed *the angle at which a reddish hue returns* (angle of circulatory sufficiency) will be found to vary considerably. In some cases it will be necessary to depress the limb to the horizontal before evidences of return circulation are manifest. The angle of circulatory sufficiency would then be 90 degrees. In many cases of arterial disease the estimation of this angle is a valuable adjuvant not only in the recognition of the extent of the circulatory disturbance but also in prognosis.

5. Absence of Pulsation as an Indication of Arterial Occlusion. We should be able to feel the femoral, posterior tibial, popliteal, and dorsalis pedis arteries pulsating in almost all individuals who possess patent arteries. In rare cases the dorsalis pedis may be aberrant in its course and therefore not palpable, or neither the dorsalis pedis nor popliteal may be accessible to the touch because of the stoutness of the patient.

To palpate the popliteal satisfactorily the patient is placed on his abdomen, lying prone. The leg is held at right angle, that is, vertical, the patient being asked to relax the hamstring muscles.

The artery is then sought in the upper half of the popliteal space, just outside of the semimembranosus and semitendinosus tendons, the fingers being pressed downward against the femur. In the upper extremities, the radial, ulnar, and brachial and axillary arteries should be examined for pulsation.

The absence of pulsation is, as a rule, an indication of occlusion at the point palpated, although in rare instances postmortem dissections have shown that the site of obliteration is somewhat higher up.

6. Reactionary Hyperemia, Rubor, or Reactionary Erythromelia. By this term we mean an *induced rubor* that manifests itself in the pendent position of the foot after the limb has been previously elevated to the vertical. It is a physiological phenomenon that ischemia, or blanching of a limb artificially produced by an Esmarch or Martin bandage, will be followed by sudden dilatation of the capillaries of the peripheral parts when the circulation is allowed to return. So, also, blanching will occur in a leg whose larger arteries are occluded on mere elevation 60 to 90 degrees above the horizontal without the use of any artificial means. When such a blanched limb is then depressed to the pendent position a similar induced or reactionary rubor will become manifest. This well-known manifestation may be invoked in the examination of cases in which impaired circulation due to arterial occlusion is suspected. It will be found particularly useful in cases of thrombo-angiitis obliterans, although also demonstrable in other cases of organic vascular disease. In early cases it is especially valuable, for it may be present long before the chronic condition of *rubor* or *erythromelia* develops.

With this introduction I may be permitted to give a brief survey of the pathology of the disease, pointing out the histological lesions characteristic of the various stages of thrombo-angiitis obliterans, and also calling attention to the facts that point to the inflammatory nature of the disease and to those observations that suggest that we are dealing with a process of microbial etiology.

In 1908 I pointed out that the name endarteritis obliterans as applied to thrombo-angiitis obliterans should be discarded, since the occlusive lesion is a thrombotic one, affecting arteries as well as veins of the extremities, and that it is independent of atherosclerosis or arteriosclerosis.

My investigations, which included a thorough pathological and histological study of the vessels in 45 amputated lower extremities, 1 upper extremity, and 25 pieces of superficial veins resected and exsected from the lower and upper extremities during attacks of so-called migrating phlebitis, have demonstrated that when the patient comes to the physician for observation the larger arteries, and often the larger veins, are completely obliterated.

As a rule the plantar vessels, dorsalis pedis and many of its branches, anterior tibial, posterior tibial, peroneal and sometimes the popliteal are already completely closed, although any one or more of these vessels may escape. One or both the venæ comites may partake of the same lesion. The obturating tissue is for the most part representative of or indicative of a healed lesion, or the end-stage of a process whose incipiency is marked by an acute inflammation of the vessel wall, with consecutive, red, occlusive thrombosis of the affected vessel. It is only in rare instances that the early stages of the vascular lesion are found in the deep vessels, but in superficial veins when they are affected with the lesion of migrating or thrombophlebitis, the early or acute stage of the disease can be studied.

Gross Pathology. The deep vessels of the amputated legs regularly show an extensive obliteration of the larger arteries and veins. Besides this there are two other lesions which vary greatly in their intensity, namely, the peri-arteritis and the arteriosclerosis. The appearance of the vessels on gross section depends upon the age of the occluding process. Usually the vessel is seen to be filled with a grayish or yellowish mass that can be distinctly differentiated from the annular wall of the vessels, and that appears to be pierced at one or a number of points by an extremely fine opening through which a minute drop of blood can be squeezed. Such obturating tissue is firm in consistency and does not at all resemble the crescentic or semilunar occluding masses typical of arteriosclerosis. The vessel itself is usually contracted, so that its wall appears somewhat thickened. This picture is characteristic of arteries or veins which are the seat of a very old obliterating process, and is to be found most frequently in the peripheral portions of the vessels, although at times this type of lesion may extend throughout the whole length of the vessel from the dorsalis hallucis into the popliteal.

As we trace certain of the obliterated arteries or veins upward, we are apt to meet with a change in the character of the obturating tissue. Frequently it becomes softer, more brownish in color, and terminates abruptly in the lumen of an apparently normal vessel; at other times the brownish tissue gives way to soft, reddish masses which are evidently the results of recent thrombosis. In some cases this thrombotic process occupies large portions of the vessel's course; in others it is of short extent and terminates in a long cone of recent thrombus.

The veins share equally with the arteries in the lesion of occlusion. In some cases the veins are more extensively involved than the arteries, and this is particularly true of the collaterals of the posterior tibial, which are often closed when the anterior tibial veins are open. As for the arteries, we usually find an obliteration of a part or of the whole of the anterior tibial; occlu-

sion of the dorsalis pedis, and dorsalis hallucis, of the posterior tibial and plantar vessels, with or without involvement of the peroneal. Sometimes the anterior tibial is practically normal in its upper half or upper two-thirds. More rarely a large portion of the dorsalis pedis is open, with the beginning of the occlusion in the upper part of this vessel or in the lower part of the anterior tibial.

Besides the lesion of occlusion there are two other striking changes, namely, a certain amount of arteriosclerotic thickening and peri-arteritis. Arteriosclerosis is absent in the younger cases; when present it is never pronounced except in those rare instances in which the patient has suffered from the disease for many years, and has reached the age of forty or more. As a rule, we note but a very slight degree of whitening or thickening of the intima, here and there, in the patent portions of the vessels. In a very few cases small atheromatous patches are present.

A much more interesting and more important change is the fibrotic thickening of tissues immediately about the vessels. Wherever the vessels are occluded there is apt to be an agglutinative process which binds together the artery and its collateral veins, and sometimes also the accompanying nerve, so that liberation of the individual vessels by dissection is difficult. The adhesive condition is due to fibrous tissue growth and varies considerably in its amount. The peri-arterial fibrosis varies, sometimes being almost absent, at other times so great that isolation of the vessels or nerves becomes impossible and the vascular structures make up one dense rigid cord.

Histopathology. The lesions may be considered in two stages: (1) the healed or organized stage, and (2) the acute or incipient stage of thrombosis. Between the earliest alterations in the deep arteries and veins and superficial veins and the finished product there are a large number of intermediate pictures that illustrate the metamorphosis of the obturating clot into the intravascular cicatrix.

1. *Healed or Organized Stage.* The most common lesion is a total obliteration of the lumina of arteries and veins by connective tissue. Histologically this may be extremely varied in the general appearance, but each picture can be interpreted correctly as having its origin in the lesion of occlusive thrombosis. This obturating connective tissue usually harbors numerous small vessels, pigment containing hemosiderin, and a fair amount of connective-tissue cells. The canalizing vessels when they become dilated form smaller or larger sinuses, giving the fenestrated or cribriform lesion seen on microscopic section of the vessels, or when the canalizing vessel becomes eccentrically placed, and sufficiently large, this sinus is responsible for the appearances which have been incorrectly interpreted as the product of an endarteritis obliterans.

Elastic-tissue stains demonstrate characteristic differences between this process and arteriosclerosis. Thus the region of the organized clot is almost completely free from elastic tissue. The small amount which is present is concentrically disposed about the new-formed vessels.

Still more suggestive and instructive is the finding of various stages of the disease in different members of the same vessel sheath. Thus in one of the lantern slides shown a large artery affords a view of the old lesion as well as one of its venæ comites. Another accompanying vein, however, is in the "acute" stage of the disease, a smaller venule or satellite being in the intermediary stage, where certain "miliary giant-cell foci" make their appearance. Such pictures not only reveal the thrombotic nature of the disease, but also present an argument in favor of the following two assumptions: that the disease begins with an inflammatory lesion attended with occlusive thrombosis, and that it affects the arteries and veins in a sort of relapsing fashion, very much in the same manner as in the veins in migrating phlebitis.

The termination of the occluding tissue in arteries and veins is often seen in the form of a rounded, convex projection looking upward (cephalad) and lying in practically healthy vessel wall. At other times the old occluding tissue is capped by an additional clot which rises in pyramidal fashion ending by a long capering extremity.

2. *The Acute or Specific Lesion.* The early lesions are so characteristic histologically that their appearances are practically specific for thrombo-angiitis obliterans and may permit the pathologist to make a diagnosis of the disease. They are rarely to be seen in the deep vessels for the reason that patients do not allow amputation until the disease has lasted for months or years. However, they can be well studied when these are the seat of the typical migrating phlebitis, and have been shown by me to be identical with the acute lesions in the deep vessels.

The earliest changes appear to be the usual evidences of an acute inflammatory process involving all the coats of the vessel. The media, adventitia, and perivascular tissues are infiltrated with polynuclear leukocytes and the lumen of the vessel is completely filled with red clot. In the peripheral portions of the clot, larger or smaller foci of leukocytes (purulent foci) begin to form, whose growth occurs by virtue of immigration of leukocytes. Then certain peculiar giant-cell foci develop and are characteristic. They contain giant cells, endothelioid cells or angioblasts and numerous broken-down leukocytes. These foci then undergo connective-tissue replacement. The giant cells gradually disappear; numerous small vessels are formed, the final product being a fibrous nodule containing vessels and some pigment. In the rest of the occluding clot the organizing process is somewhat different, resembling

that which characterizes the organization of blood clot in other thromboses.

In short, the lesions in thrombo-angiitis obliterans are in chronological order: (1) an acute inflammatory lesion with occlusive thrombosis, the formation of miliary giant-cell foci; (2) the stage of organization or healing, with the disappearance of the miliary giant-cell foci, the organization and canalization of the clot, the disappearance of the inflammatory products; (3) the development of fibrotic tissue in the adventitia that binds together the artery, vein, and nerves.

## A CONSIDERATION OF THE TREATMENT OF PERIPHERAL GANGRENE DUE TO THROMBO-ANGIITIS OBLITERANS, WITH REFERENCE TO FEMORAL VEIN LIGATION AND SODIUM CITRATE INJECTIONS.[1]

By Nathaniel Ginsburg, M.D.,
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The surgical treatment of impending or actual gangrene of the extremities due to pathological changes in the peripheral bloodvessels, termed thrombo-angiitis obliterans by Buerger, embraces a number of procedures which attempt to increase the circulation in the impaired limb. The successful application of a surgical principle to cure a pathological process presupposes the possibility of either totally extirpating the diseased area or structure, or the correction of a departure in normal organic function until such time as may be required for tissue restoration or regeneration to take place.

Buerger's convincing demonstration of the true pathological entity of the disease which bears his name leaves no doubt as to the presence of the extensive bloodvessel changes which have already taken place when these cases are first observed. In most instances the disease has progressed to the point of impending gangrene or actual digital death, and all surgical measures for relieving the great suffering and distress of these patients are really only palliative in nature.

A considerable amount of experimental laboratory work, performed abroad and in this country, for the purpose of establishing the value of arteriovenous anastomosis in the treatment of this disease, has proved rather conclusively that true reversal of the circulation in the affected limb cannot be accomplished, even though Carrell and Guthrie successfully established in their labora-

[1] Read before the College of Physicians of Philadelphia.

tory experiments the possibility of conducting arterial blood to the peripheral capillaries by way of the veins.

Arteriovenous anastomosis, femoral vein ligation, section of the sympathetic fibers about the femoral vessels, multiple ligations of the superficial varicose veins in the affected limb (Lilienthal), high amputation and intravenous saline injections have been proposed and performed by observers all over the world in their efforts to combat the circulatory failure in the affected limbs. In addition to these measures, every conceivable form of local treatment to stay the impending or spreading gangrene has been employed with almost uniform failure in the final results obtained.

Willy Meyer has recently contributed an important article upon the employment of conservative measures in the treatment of peripheral gangrene, and refers to the interesting work of von Oppel, who has performed femoral vein ligation in these cases, with the belief that the peripheral venous stasis thereby induced from the anatomical point of view has the same relative value as arteriovenous anastomosis.

This latter operation, often incorrectly termed reversal of the circulation in the affected limb, was first performed by San Martin Y Sastrustigui in 1902, and has been exploited by Coenen, of Breslau, Wieting, of Constantinople, and many others both abroad and in this country. The operation owes its conception to the successful end-to-end suture of bloodvessels practised by Carrell and Guthrie. As originally performed it consisted in an end-to-end anastomosis in Scarpa's triangle between the femoral artery and vein, attended by section of each structure and ligation of the proximal end of the vein and of the distal end of the artery. Later, lateral arteriovenous anastomosis of these vessels in the thigh was suggested by Bernheim and Stone, of Baltimore, with ligation of the femoral vein proximal to the site of the anastomosis as a necessary and important feature of the operation. As a rule the anastomosis in the thigh was made below the profunda femoris vessels.

The final results obtained and a study of the philosophy of this surgical procedure lead to the conclusion that the operation is founded upon a faulty anatomical and physiological basis. Guthrie has stated that he did not believe that arteriovenous anastomosis successfully applied to animals in the laboratory should be employed in the human being suffering from advanced vascular disease of the type under discussion. Stetten, of New York, in stating his views regarding the futility of arteriovenous anastomosis in the treatment of impending gangrene of the lower extremity, supplemented his condemnation of this operation by reporting convincing proof based upon injection experiments and dissections of the bloodvessels in amputated limbs. His studies have been confirmed by Horsley, of Richmond, whose conclusions are in unity

with those of Coenen and Wiewiorowski who likewise concluded, in 1911, that the operation was unsound and dangerous.

Stetten studied 136 published arteriovenous anastomoses, or attempts at this operation. He found that 30 deaths resulted immediately or shortly following the operation, and 11 patients died after amputation following the performance of the anastomosis. The immediate death-rate therefore was 30 per cent., and of those that did not die, 45 required amputation. Therefore in more than 72 per cent. of the cases arteriovenous anastomosis had either failed or could not be accomplished, owing to the technical difficulties encountered. Insufficient lumen of the vessels or advanced arteriosclerotic changes precluded even a successful attempt at bloodvessel suture in many of the failures reported.

If any value attaches to arteriovenous anastomosis it is probable that the good resulting from the operation is solely due to the ligation of the femoral vein on the proximal side of the newly created opening, thereby practically accomplishing in principle a pure femoral-vein ligation. Meyer has recently reported a case of Buerger's disease with involvement of the base of the big toe and adjacent metatarsal bone in which he performed arteriovenous anastomosis, with a good result. An analysis of the history of his case compares so closely with one of my own, in whom only ligation of the femoral vein was performed, as to make the cases identical from the stand-point of involvement and successful end-result achieved. In this instance the success attending the operation is credited to the so-called "reversal of the circulation" which is believed to have resulted.

No doubt there have been many failures following arteriovenous anastomosis for peripheral gangrene which have not been reported, and I can personally add to the long list of failures one of my own, of which no previous mention has been made.

It is apparent that arteriovenous anastomosis has no place in the treatment of this disease, since the high percentage of failures will always exist, owing to the technical difficulties attending the operation and the advanced state of the disease when the operation is performed. It must be borne in mind that while these patients suffer principally from peripheral vascular disturbances they are also poorly nourished and bear other evidence of a clinical syndrome of which their peripheral trophic disease is the most striking feature.

Femoral-vein ligation is a simple technical procedure and will certainly and effectively produce circulatory stasis, and thereby bathe the affected limb in more blood than is present when no retardation of the venous system exists. Since Buerger has shown that the principal changes are largely confined to the peripheral arteries the tissue asphyxia resulting from deficient oxygenation is not overcome by this operation. This operation has been per-

formed by von Oppel, Coenen, Lilienthal, Horsley and others and by myself in 4 cases. If desirable it may be done under local anesthesia. In effect, this operation has, no doubt, been performed many times, since the examinations after death, following arteriovenous anastomosis, have shown thrombus occlusion at the newly created bloodvessel stoma, or contraction amounting to a complete functional closure of the opening between the artery and the vein.

Independently, or in conjunction with this operation, the employment of intravenous injections of a saline solution, either 2 per cent. sodium citrate or Ringer's solution, has been carried out, following the suggestion of Kogo and Mayesima, of Japan. They reported 15 cases of this disease treated with injections of a saline without femoral-vein ligation in the surgical clinic of Professor Ito. Employing a viscosimeter for testing the blood they concluded that there is an increased viscosity in the blood of patients suffering from this disease. Based upon this observation came the conclusion to employ sodium citrate solution for intravenous injection in order to decrease the degree of viscosity.

Garbat, of New York, has recently stated and proved that multiple injections of 2 per cent. sodium citrate solution into the veins of the human organism do not have a deleterious effect, and I have also employed multiple injections of this solution in varying amounts in conjunction with femoral-vein ligation.

Other than the mere mention of a single case (Lakeside Hospital in Cleveland) I have been unable to find any reference to the results obtained by section of the sympathetic fibers about the femoral vessels. Many cases of thrombo-angiitis obliterans have as a concomitant feature of the symptom-complex pronounced vasomotor disturbances; but it is difficult to conceive how the advanced thrombus occlusion of the bloodvessels can be antagonized by section of the vasomotor fibers surrounding the large bloodvessels in the thigh.

When one witnesses the excruciating pain which these patients suffer, with the attendant loss of sleep, often uncontrolled by sedatives, the temptation is quite strong to perform early amputation before or at the first evidence of peripheral digital death. Haste in amputating, without first employing conservative measures, will often sacrifice extremities which may have been saved. In many instances, even though palpable pulsation of the vessels is wanting, patients will carry limbs for years with lessened pain and arrested disease after one or more toes have been lost. If the process is rapidly gangrenous and conservative measures are contraindicated, early high amputation should be advised to obviate the greater dangers of delay.

These cases haunt the hospitals for months and years, and one surgeon will begin by amputating a toe, and after having visited

many institutions the final termination of the disease in the extremity or extremities involved will be high amputation by a surgeon in another institution. The first operation is not always the last, and if a follow-up system is employed in these cases, one is not surprised to learn that physical usefulness usually ceases with the early onset of the disease. One patient who came under my observation had had his first operation at the hands of Mixter, of Boston, fourteen years previously. Then followed successive operations by many surgeons in various institutions, and he finally entered Mount Sinai Hospital with two unhealed stumps a few inches below Poupart's ligament. Employing spinal anesthesia his long-continued suppuration was finally terminated. He had been an inmate of hospitals almost constantly since his first operation, and between his cigarette habit and the use of drugs to which he had become addicted, due to his great pain, he was in a restful state of mental apathy.

Another patient, whom I saw from the earliest physical appearance of the disease, a man, aged forty years, a carpenter by trade, suffered first the amputation of the toe of one leg, and then the leg itself was removed just below the knee, with long-continued suppuration and final slow healing of the stump, preserved for an artificial limb. A tourniquet was not required and there was scarcely any spurting from the tibial vesssels when the amputation was performed. A year later he developed involvement of the big toe of the other leg, followed by slow and progressive involvement of the foot, refusing operation, until finally driven by the fearful pain in the gangrenous foot and leg to have removal of the limb in another hospital.

With reference to local treatment we have tried various saline foot-baths, heat, Bier's hyperemia, electrotherapy, and many drugs locally to the diseased parts, none of which have appeared to have any specific value. Much has been claimed for ascitic fluid applied locally to the involved digits. I personally have amputated limbs where free use of ascitic fluid was made and have never seen any benefit result from its employment.

During the period of life in which this tragic disease is commonly observed in the male adult the female is engaged in repeated pregnancies and thereby suffers from constant engorgement of the lower extremities as the result of increased pelvic pressure due to the gravid uterus. This might possibly be a factor of some significance in determining the discrimination of the disease in favor of the male sex. Most patients suffering from this disease are inveterate cigarette smokers, using a cigarette of cheap tobacco rolled in paper of very poor quality.

Among the causes assigned to the production of this disease are infection (Buerger), some underlying toxemia, and altered quality of the blood (Meyer). The determination of the causative factors

producing a disease of this type, having sharp limitations with reference to age, habits, nativity, and sex, calls for more determined and prolonged study in order to elicit a method of treatment more successful than any now at our disposal.

With reference to femoral-vein ligation the important facts in 4 cases are as follows:

CASE I.—W. K.; male, aged fifty-three years; Russian; fruit dealer; admitted to the Jewish Hospital May 21, 1916. Chief complaint: excessive burning pain in the right first and second toes. In December, 1914, the patient felt a burning sensation in the right big toe associated with constant severe pain, making sleep impossible. The toe became blue and extremes of temperature applied to the foot increased the pain. Electrotherapeutic treatment in the hands of the late Dr. W. L. Rodman improved his condition and the pain was lessened for a period of six months. In December, 1915, the pain and discoloration spread to all of his toes, involving the dorsal surface of the foot. Patient was born in Komnitz, South Russia, and came to this country when nineteen years of age. He began to smoke cigarettes when ten years of age, smoking ten to fifteen daily. He had typhoid fever at the age of sixteen; denies venereal disease; does not use alcohol; has worked hard all his life. He is married and the father of nine children, two of whom died in early infancy; the others are living and well. The winters are very severe in his birthplace, thirty miles from Odessa, and he was subjected to severe climatic exposure when he resided in Russia. Before he came to America he worked at a machine for about twelve years, employing both feet to run the machine. After coming to this country he peddled fruit for two years and then worked in a fish store, and finally went into the fruit business, being constantly exposed all this time to weather conditions. He has never been a big fish-eater.

Ten years ago, at the age of forty-three years, he was in the Jewish and Medico-Chirurgical Hospitals, the left foot having been amputated in the former institution for the condition which is now affecting his right lower extremity. This amputation followed multiple operations upon the foot for the relief of his condition. At the present time the pain in his right foot is persistent and unendurable without a sedative. The posterior tibial and dorsalis pedis arteries are not palpable. The mesial surface of the big toe at the first interphalangeal joint shows a trophic skin ulcer. The break in the skin is not complete. The nails of the first and second toes show marked trophic changes, the nail-bed of the second toe being the site of an ulcer of small dimensions. The dorsal veins of the foot are numerous but are fine and not distended, and the circulatory failure in the foot is marked by a line of cyanosis about 1 cm. proximal to the metatarsophalangeal joints, and the toes are mottled and cold.

May 22. 50 c.c. of 2 per cent. sodium citrate solution injected intravenously.

May 25. 32 c.c. of 2 per cent. sodium citrate solution injected intravenously.

May 26. 75 c.c. of 2 per cent. sodium citrate solution injected intravenously into the femoral vein, with coincident ligation of this vein by silk and catgut ligatures, with separate ligation of the long saphenous vein. The limb following ligation became deeply cyanotic, with intense mottling and marked diminution in temperature.

May 27. The appearance of the lower extremity is unchanged. The toes are intensely cyanotic, having a deep blue hue, and the foot is cold.

May 28. The leg is warm down to the ankle, with slight distention of the dorsal veins of the foot. The toes are less cyanotic, the blue color having given way to a purple-red hue, sharply defined at the metatarsophalangeal junction. The patient says he has less pain and slept better last night than any night since his admission into the hospital. Over the upper third of the leg there is some venous distention, an oblique vein crossing the tibia from within and outward and downward. The dependent position of the foot hanging over the side of the bed increases the reddish-blue hue of this part.

May 29. There seems to be more prominence of the dorsal veins of the foot and the color of the toes is assuming a normal red tone. The toes, however, are still cool and the lowered temperature of the part extends to the upper third of the leg. The nail-bed of the second toe is dried up.

May 31. 100 c.c. of 2 per cent. sodium citrate solution injected intravenously.

June 5. The foot is warm, there is little pain, and the venous stasis has completely disappeared. The toes are still discolored and reddish blue, but there is very pronounced improvement in the circulation of the foot.

June 6. 100 c.c. of 2 per cent. sodium citrate solution injected intravenously.

June 7. Patient's leg is much warmer, and he states that he feels less pain. Patient requested that further intravenous injections be discontinued, and at his request was allowed to go home. (Total 357 c.c. of 2 per cent. sodium citrate injected.)

August 4. The right leg is somewhat edematous, toes are cyanotic, tense, and uniformly involved in the disease. The dorsal surface of the foot is blue and very painful. There is no venous distention such as he had shortly after his operation, and apparently little permanent good has resulted from the operation. His pain has returned and is becoming severe, necessitating the constant employment of narcotics.

This case has been reported somewhat in detail because it is a typical example of a case of thrombo-angiitis obliterans relative to nativity, history, and onset of the disease, terminating in the loss of one extremity and the future loss of the other, following a total occlusion of the femoral and saphenous veins, with coincident injection of sodium citrate solution.

Case II.—M. G.; male, aged twenty-seven years, operator by trade; born in Russia. Admitted to Mount Sinai Hospital May 8, 1916. Diagnosis: thrombo-angiitis obliterans of the left foot, with the presence of digital ulceration. He was treated for many weeks in the Polyclinic and Jefferson Hospitals without relief. The details of the disease are too time-consuming to enumerate.

May 11. Ligation of the femoral vein was performed below the point of entrance of the long saphenous vein. Marked venous stasis promptly resulted, assuming the startling appearance of the case previously reported. He received daily injections of Ringer's and sodium citrate solution in large quantities from May 12 to May 19 inclusive, when he refused further injections and left the hospital against advice. The social service worker following this case traced him to another hospital and reported that amputation of the leg was necessary, owing to the progression of the disease.

Case III.—J. E.; male, aged thirty-six years; Russian; baker by trade. Admitted to Mount Sinai Hospital January 10, 1916; discharged February 8. Diagnosis: thrombo-angiitis obliterans of left foot. Patient came to the hospital with severe pain in the big toe of the left foot, which became gangrenous, the gangrene extending to the tarsometatarsal junction corresponding to this digit. The acute process was of six weeks' duration, the toe becoming gangrenous two weeks previous to admission. Patient was an inveterate cigarette smoker.

January 10. Disarticulation of the big toe and the metatarsal bone was done; the wound was not sutured and no ligatures were required.

January 14. The wound was suppurating and gangrene was apparently slowly spreading; temperature, 100° to 102°. Patient discharged February 8, with a suppurating wound and marked failure in the circulation of the foot. He was readmitted to the hospital May 31 with an unhealed wound and discoloration of the remaining toes of the left foot. The toes and dorsal surface of the right foot likewise show circulatory failure. The dorsalis pedis artery is not palpable in either foot and the veins are small and not distended.

June 3. Femoral vein ligated, with coincident injection of 100 c.c. of 2 per cent. sodium citrate solution.

June 4. Left foot is much warmer than the right; the veins are congested and the patient states that he feels more comfortable. 100 c.c. of 2 per cent. sodium citrate solution injected intravenously.

June 5. Patient is comfortable.

June 6. Patient's left foot and leg are slightly swollen, due to the venous congestion produced by the operation. Extremities quite warm to the toe-tips, with normal color and very marked distention of the surface veins of the foot. The opposite foot (right), which has not been operated on thus far, is distinctly colder than the left, and is giving much pain and discomfort, with marked cyanosis of all the toes, the big toe being especially involved. In comparison the left foot seems considerably better nourished and the result of the ligation at this time is unquestionably astonishingly good in this case. The transformation seems almost unbelievable, and the patient is considering the same procedure in the right lower limb. He has slept better and is having practically no pain in his left foot.

August 1. Patient has been at work all summer, having little pain in the left lower extremity, which is markedly swollen, the edema having increased the leg to almost twice its normal size. The nutrition of the limb at the present time is good and the progress of the disease seems arrested. The wound resulting from the removal of the big toe and the contiguous metatarsal bone has completely healed. He is now suffering from involvement of the other extremity and the problem of treatment arises again in this case.

The patient was observed on October 3, and the examination of his left lower extremity showed considerable diminution in the size of the limb as the result of stasis resulting from ligation of the femoral vein. He is suffering practically no pain in this limb, and complains of pain and feeling of fatigue affecting the right lower extremity.

Case IV.—M. T.; Russian; male, aged fifty-eight years; a truck driver in his native land, becoming a huckster upon his arrival in this country. Began smoking cigarettes at twelve years of age, averaging ten to twenty daily, and has been a heavy whisky drinker for many years. Married, had twelve children, eight of whom are living and well. Was in the Russian army for six years. Father died at ninety, mother at seventy-five. Family history negative in relation to the present disease. Ten years ago, when forty-eight, patient suffered from pain in the calves of both legs, compelling him to stop work at intervals. This pain continued until nine months ago, when his condition became so aggravated that he had to cease working. He has had a reddish-blue discoloration of the toes of both feet for the last six years and ulcerated areas over the anterior surface of both legs for the past five years, with failure of healing accompanied by great pain. The ulcers are trophic and pulsations in the vessels of the foot are absent. He was treated in the Polyclinic Hospital for six weeks by Dr. George P. Müller, who believed that the case was one of thrombo-angiitis obliterans, and submitted the patient to saline injections. This case was one

in which there was circulatory failure, but owing to the age of the patient and the atypical location of his trophic ulcers I do not know whether he can be termed a typical case of thrombo-angiitis obliterans, although the examination of both feet confirmed the proper classification of the disease as one of this type.

May 31. 50 c.c. of 2 per cent. sodium citrate injected intravenously.

June 3. 100 c.c. of 2 per cent. sodium citrate injected intravenously into the femoral vein, accompanied by ligation of this vessel. The leg immediately assumed an intensely purple hue, with a most pronounced venous stasis of the limb below the knee-joint. The patient was in a state of shock at the conclusion of the operation, with subnormal temperature and rapid pulse, and cried out because of intense pain in the limb.

June 4. Suppression of urine was marked, only one-half ounce having been recorded in the past twenty-four hours. The right lower limb is now mottled and markedly cyanotic below the knee-joint. The left leg still remains cold and blue. Anuria is complete, the patient having the odor of urine on his breath, is vomiting, and has a subnormal temperature.

June 5. Patient's condition remains the same. There is very marked or total venous obstruction of both lower extremities, suggestive of a thrombus of the inferior vena cava. Patient died on this day, apparently of suppression of urine.

He was a poor operative risk, and undoubtedly not a good case for femoral-vein ligation.

Femoral-vein ligation based upon the experience of these few cases is an operation of doubtful value, since only 1 of the 4 patients showed any improvement following its performance. This case has unquestionably improved to the point of security of the limb in which the venous current was obstructed. Involvement of the other leg is now taking place and the value attaching to the procedure may be still greater in the future, since it may preserve one of his extremities.

The operation is a hazardous one and may cost the life of the patient, as occurred in Case IV of my series. If ligation is done the ligature should always be placed below the entrance of the long saphenous vein into the femoral vein, thereby preserving some collateral venous circulation in the affected limb. Following this operation there is developed a large posterior femoral vein passing from the popliteal space as a tributary to the sciatic or inferior gluteal vein.

In one of my cases ligation had no effect whatever in retarding the progress of the disease, and even failed to produce venous stasis in the affected extremity. It was a convincing example of how greatly impaired was the arterial distribution to the peripheral parts in the affected limb, and proved that the problem cannot

be attacked except by dealing with the arterial element in this disturbed circulation.

I believe that the poor arterial circulation present is much better than the results attained by any of the proposed surgical measures to increase the circulation in the involved extremity.

We must bear in mind that this disease is almost invariably seen in its terminal stages and that surgical measures are simply palliative in nature and cannot achieve a positive cure. My own experience with the injection of the sodium citrate solution has not been very satisfactory, since I have noted little improvement in the patients, and have found it difficult to continue the injections over a long period of time, since so little early relief has followed them. This experience is in agreement with the later reports dealing with the value of saline injections in this type of peripheral gangrene. Much of the early improvement noted by other observers has only been temporary, and lasting results have not been attained.

## THE NEWER CONCEPTS OF THE NEUROSES: AN ESTIMATE OF THEIR CLINICAL VALUE.[1]

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I have tried to put to a kind of test some of the ideas concerning the neuroses that have seemed worth while and have endeavored to see what truth there is in them. In doing this I have attempted to be unprejudiced and, as far as one may with clinical material of a varied kind, to adopt a detached and unbiased attitude.

The questions I have set myself to answer are: (1) what are the really important theories which cluster about the attempt to explain the neuroses; (2) of what use are they; (3) what remains after the untrue and useless are set aside.

What is to be understood by the term "neuroses?" They are clinical pictures of diseases which are primarily psychogenic in origin and in manifestation, the objective symptoms of which do not conform to the known laws of anatomical distribution or physiological function, and in which the intelligence is not sufficiently affected to be included within the limits of the psychoses, and in which conduct is kept within the limits of what is called normal.

This definition as set forth here is intended merely to delimit a large class of nervous diseases from the organic on one side and from

[1] Read by invitation before a combined meeting of the Chicago Medical and Chicago Neurological Societies. The introduction is here omitted.

the purely mental on the other, serving to section them off for the purpose of further discussion.

If certain general notions are kept in mind it is useful to think of such diseases as conforming to certain natural divisions into which they almost automatically fall.

The first of these notions is that a rigid classification is impossible and that pure types are rare.

The second is that certain of the neuroses deal chiefly with phenomena that are conscious and certain others with phenomena that are unconscious (or subconscious or foreconscious, whatever term is used).

In this sense the following tentative classification would seem to be of use:

1. Neurasthenia. A fatigue neurosis in which the elements of fatigue and irritability are the primary factors and in which all symptoms are capable of interpretation from these two points of view.

2. Hypochondrosis, in which all symptoms can be referred to perversions in interpretation of afferent sensory stimuli. To these the patient ascribes the evidence and proof of disease.

3. Psychasthenia, which is a congenital state of indecision and doubt, chiefly based upon the fear of the consequence of choice.

These three then are, according to this view, purely conscious in origin and manifestation. To their consideration the patient can bring his intelligence, his experience, and his insight.

4. Hysteria, in which there is a disassociation of consciousness, and in which the manifestation of disease are sharply separated from their origin, and in which conscious synthesis is wanting.

5. Compulsion neuroses, in which the force of an idea becomes the dominating factor in the patient's existence, driving him to the performance of acts contrary to his wishes and to his interest, and which by virtue of his struggle at neutralization or control, various phenomena result, such as fear, attacks of anxiety, etc.

Toward the orientation of these various types of neuroses four important sets of hypothesis have been adduced. They are in their order of importance:

(*a*) Freudian psychology.
(*b*) Janet disassociation of consciousness.
(*c*) Babinski group of ideas.
(*d*) The theory of congenital or acquired inadequacy.

In a rough sort of way the newer conceptions of the neuroses may be said to date from the time Janet, a trained psychologist, began to apply laboratory methods to the investigation of the neuroses in Charcot's clinic at the Salpêtrière.

From this clinic Freud received the impulse which led him to elaborate the psychological principles prevalent at that time. It was about 1900 that the result of this work began to penetrate into

the neurological world. No neurological epoch has been so fruitful in results and shown so much interest and effort on the subject of the neuroses as this period.

I am not concerned with origin or history, and it makes little difference whether to Freud or someone else credit or discredit should be given for the ideas which have aroused so much conflict. The names are therefore only important as they serve to identify this or that formula with which we are concerned.

By far the most ambitious attempt to solve the total problem of the neuroses is that of Freud. This attempt is concerned with the finding of a common etiology, the establishment of certain basic psychological principles—a mechansim of investigation which contains at the same time its chief therapeutic measure. In a paper of this sort it would be impossible to attempt any critical estimate of the Freudian psychology as such, nor does it seem to me that any approach to its final judgment in respect to its ultimate truth is at present possible. A system which aims at the psychological determination of so many aspects of mental abnormalities as this must, in the nature of things, contain many errors and wrong points of value. How much truth there is contained in it is, I believe, less important than how great is its usefulness and how frequently are its accepted facts capable of being put to the test of actual experiment.

It is obvious that a worker in the field of the neuroses need not be bound by any limitation set upon his activities in trying out a theory, so whether the proper Freudian attitude is present or not is of less consequence than that the usual critical atmosphere in any serious investigation be preserved. With this notion in view the first difficulty in the Freudian psychology makes itself felt by the lack of proof that the sexual etiology is common to all the neuroses. Granting as wide a conception of the term sexuality as is possible, the definite fact remains that there is found no such etiological uniformity as the Freudian literature insists upon. By no process is it possible to reveal a uniform and a persistent sexual etiology.

The sexuality conception of Freud may be very briefly outlined as follows:

In his early publications, from 1894 on, he divided the psychoneuroses that were due to sexuality into two groups: (1) neurasthenia and the neuroses of anxiety which were due to existing sexual troubles, and (2) hysteria and the obsessions due to sexual traumata of childhood period to the age of eight years.

In his later publications Freud seems to admit that too much emphasis had been placed upon these infantile impressions and that some of the histories obtained from psycho-analysis were imaginary. The sexual constitution of the infant now occupies a more important place and the term libido comes into prominence. According to this view the child has in him all the forms of sex perversion which

are met with in the adult, and is a polymorph pervert. At the age of puberty the auto-erotic child transfers his sex objective to one of the opposite sex.

There are three forms that can be followed:

1. The infantile tendency may be perverted and be recognized by the object as a sex invert or pervert.

2. The infantile tendency is normal or otherwise and may be repressed and hidden by the object to crop up after puberty as a psychoneurosis.

3. The sexual tendency may be directed toward the purely psychical end in art, science, and mysticism, and this process is termed sublimation.

The technic of this investigation is usually that of psycho-analysis, developed by a thorough acquaintance as might be acquired through the literature, through contact with well-known Freudian students and by actual experience and study. The criticism that is likely to be made to a negative conclusion of this kind is always based upon the insufficient technical ability with the method itself—a criticism which, unfortunately, can never be answered directly. To this conception this question can be put: Why is it if psycho-analysis has proved itself so excellent a device for the investigation of the neuroses, has proved its therapeutic worth so often, the mere fact that it does not in most instances reveal the expected etiology be taken as a proof that its technic is at fault? It has been said that if the sexual etiology of the neuroses is not admitted that the whole Freudian fabric falls to the ground, and if in a psycho-analytical investigation of a case the sexual factor is not revealed, the proof is complete that the study has been made with a technic that is faulty and insufficient. Such statements seem of less consequence than the fact that the method itself is of great value and has been responsible for a very definite advance in the investigation and treatment of the neuroses.

The criticism which confronts any attempt to delimit the Freudian doctrine from the point of view of its utility and adaptability is always based upon the fact that the critic is not an accredited Freudian and that he is not the technical master of the method itself. I shall forestall this by frankly admitting both charges, with the plea that so valuable a body of doctrine must contain sufficient truth to admit of partial belief and partial mastery.

It is necessary to indicate now what are some of the other essential factors that form the so-called Freudian psychology. As I have said, Freud has set himself the extraordinary task of building around the idea of sexuality and its perversions an etiological mechanism which should provide for all the neuroses a common causal impulse. This, it is to be understood, was in no sense a preconceived idea of Freud himself. In the course of a series of cases studied by means of psycho-analysis he became convinced that this was true. This

etiological conclusion would be considered as the most significant item in the list of necessary postulates of the Freudian theory.

Probably the next important fact would be the freely admitted proposition that practically all the neuroses, with the exception of the neurasthenic group, are unconscious or subconscious phenomena. As a necessary corelation to the etiology spoken of above, there has developed the important idea that, owing to the necessity of providing some means by which the sexual impulse may be controlled for the apparent benefit of the individual and society, a conflict develops through the mechanism of suppression. It is this conflict which is the logical consequence of the effort to keep back that which is not in harmony with the individual, or rather the conventional ideas of action and of thought, which civilization demands of him. Such group ideas, called constellation, associated with suppression of painful and emotional states, tend to be repressed or thrust back into consciousness. To this the term "complex" has been given. Such a complex tends to expression, and in so doing gives rise to symptoms which are at times the motor or sensory evidence of the conflict objectivated in the clinical picture known as hysteria.

These, then, form the third group of the essential formulæ of the Freudian doctrine. Sexual infantile trauma, repression with its great variety of mechanism, the establishment of the conflict, the notion of a complex and its need of expression, such an expression taking on the form of lawless and half-understood external manifestations. The fourth group of Freudian facts is the mechanism of investigation and treatment—that is, the psycho-analysis, which includes the use of the interpretation of dreams as an essential medium for the study of the repressed psychical material.

A discussion of psycho-analysis as a method need not detain us here, but the dream with its symbolic language and its interpretative value are of primary interest. To no part of the Freudian doctrine has greater significance been given than this, and by many it is regarded as Freud's lasting contribution to psychology.

Associated closely with the dream interpretation is naturally the conception of wish-fulfilment as an initiative of all dreams. There are many aspects of the dream problem which cannot here be mentioned, but a few are essential to keep the narrative thread of the discussion.

It is obvious that if a dream contains both repressed and unrepressed material the story of the dream is not so simple as the dreamer imagines. The content is therefore of two parts, manifest and latent. It is chiefly with the latter that the main interpretative effort is concerned. By a process identical with psycho-analysis the latent content is analyzed out with the object of seeing through such dream activities as condensation, distortion, over-determination, displacement. These are terms used to express the manifestly absurd pictures with which dreams are filled. All

this seems to serve the purpose of defense, as it were, a protective mechanism to save the dreamer from the realization of what he is really dreaming about. Much of the language of dreams is symbolic in the sense that symbols are at the same time a mirror of infantile and primative speech and serve to express events and experiences incapable of personal conscious understanding. It is the interpretation of the symbolic language into terms readily appreciated which enables the interpreter to see very deeply into his patient's mind.

These, then, as I conceive them are the important facts in the Freudian psychology.

It is apparent that a method of investigation is of itself valuable only as it furnishes a mechanism by which truth can be reached, and that whether the final conclusion is always identical or not is of minor importance; but what does matter is the evidence of the value in suitable cases by the use of a method of this kind. Laying aside, therefore, the questionable nature of the root idea, included under the term sexuality, as limiting the aim and final goal of all psycho-analytic efforts into the neuroses, in what way are we the gainers through the immense labors of this band of enthusiastic investigators?

It might be well to call attention to one important fact which is commonly lost sight of when the neuroses are discussed; that is, with the closer study of the neuroses as mirrored in the Freudian literature greater attention and emphasis are necessarily given to the acquiring of data and to the study of the intimate mechanism of their occurrences. Paralleling this very important advances have been made in the technic of clinical investigation of organic disease as well. There results, then, two opposing tendencies, a clear and more definite determination of the neuroses, with the gradual subtraction from this class to this or that class of organic disease, and, on the other hand, a much more intensive effort directed to the understanding of the decreasing material included under the term neuroses. For example, the neurasthenic class has become enormously lessened by two important clinical points of view. The role of tuberculosis in causing fatigue states, which were formerly called neurasthenia, and the point of view which sees in many neurasthenias the prodromal state of various functional psychoses.

In this way the material open for Freudian therapy is capable of a good deal of warranted selection both as to type and to individual suitability.

The effect of all this effort may be easily seen in the histories of patients as they pass through the clinic or hospital service. Whether the neurologist or his staff are accredited Freudians or not there is to be observed a curious automatic insistence on the part of the clinical inquirers in regard to the presence of psychical traumata

etiological conclusion would be considered as the most significant item in the list of necessary postulates of the Freudian theory.

Probably the next important fact would be the freely admitted proposition that practically all the neuroses, with the exception of the neurasthenic group, are unconscious or subconscious phenomena. As a necessary corelation to the etiology spoken of above, there has developed the important idea that, owing to the necessity of providing some means by which the sexual impulse may be controlled for the apparent benefit of the individual and society, a conflict develops through the mechanism of suppression. It is this conflict which is the logical consequence of the effort to keep back that which is not in harmony with the individual, or rather the conventional ideas of action and of thought, which civilization demands of him. Such group ideas, called constellation, associated with suppression of painful and emotional states, tend to be repressed or thrust back into consciousness. To this the term "complex" has been given. Such a complex tends to expression, and in so doing gives rise to symptoms which are at times the motor or sensory evidence of the conflict objectivated in the clinical picture known as hysteria.

These, then, form the third group of the essential formulæ of the Freudian doctrine. Sexual infantile trauma, repression with its great variety of mechanism, the establishment of the conflict, the notion of a complex and its need of expression, such an expression taking on the form of lawless and half-understood external manifestations. The fourth group of Freudian facts is the mechanism of investigation and treatment—that is, the psycho-analysis, which includes the use of the interpretation of dreams as an essential medium for the study of the repressed psychical material.

A discussion of psycho-analysis as a method need not detain us here, but the dream with its symbolic language and its interpretative value are of primary interest. To no part of the Freudian doctrine has greater significance been given than this, and by many it is regarded as Freud's lasting contribution to psychology.

Associated closely with the dream interpretation is naturally the conception of wish-fulfilment as an initiative of all dreams. There are many aspects of the dream problem which cannot here be mentioned, but a few are essential to keep the narrative thread of the discussion.

It is obvious that if a dream contains both repressed and unrepressed material the story of the dream is not so simple as the dreamer imagines. The content is therefore of two parts, manifest and latent. It is chiefly with the latter that the main interpretative effort is concerned. By a process identical with psychoanalysis the latent content is analyzed out with the object of seeing through such dream activities as condensation, distortion, overdetermination, displacement. These are terms used to express the manifestly absurd pictures with which dreams are filled. All

this seems to serve the purpose of defense, as it were, a protective mechanism to save the dreamer from the realization of what he is really dreaming about. Much of the language of dreams is symbolic in the sense that symbols are at the same time a mirror of infantile and primative speech and serve to express events and experiences incapable of personal conscious understanding. It is the interpretation of the symbolic language into terms readily appreciated which enables the interpreter to see very deeply into his patient's mind.

These, then, as I conceive them are the important facts in the Freudian psychology.

It is apparent that a method of investigation is of itself valuable only as it furnishes a mechanism by which truth can be reached, and that whether the final conclusion is always identical or not is of minor importance; but what does matter is the evidence of the value in suitable cases by the use of a method of this kind. Laying aside, therefore, the questionable nature of the root idea, included under the term sexuality, as limiting the aim and final goal of all psycho-analytic efforts into the neuroses, in what way are we the gainers through the immense labors of this band of enthusiastic investigators?

It might be well to call attention to one important fact which is commonly lost sight of when the neuroses are discussed; that is, with the closer study of the neuroses as mirrored in the Freudian literature greater attention and emphasis are necessarily given to the acquiring of data and to the study of the intimate mechanism of their occurrences. Paralleling this very important advances have been made in the technic of clinical investigation of organic disease as well. There results, then, two opposing tendencies, a clear and more definite determination of the neuroses, with the gradual subtraction from this class to this or that class of organic disease, and, on the other hand, a much more intensive effort directed to the understanding of the decreasing material included under the term neuroses. For example, the neurasthenic class has become enormously lessened by two important clinical points of view. The role of tuberculosis in causing fatigue states, which were formerly called neurasthenia, and the point of view which sees in many neurasthenias the prodromal state of various functional psychoses.

In this way the material open for Freudian therapy is capable of a good deal of warranted selection both as to type and to individual suitability.

The effect of all this effort may be easily seen in the histories of patients as they pass through the clinic or hospital service. Whether the neurologist or his staff are accredited Freudians or not there is to be observed a curious automatic insistence on the part of the clinical inquirers in regard to the presence of psychical traumata

in the past history of the patient. This inquiry does not stop with the ordinary conventional questions, it drives back into the realm of the patient's earliest memories. It is surprising, indeed, to observe how many facts are in this way obtained and how much richer the personal story of the patient becomes. I am referring not alone to hysteria, but to all classes of patients which this paper particularly addresses itself.

The conclusion seems irresistible, therefore, that the body of Freudian doctrine has penetrated largely into the general neurological mind irrespective of personal differences of opinions as to the correctness of many of its separate units.

This then may be regarded as one of the permanent results of what I called the newer conceptions of the neuroses.

Perhaps it means merely a sharpened intelligence and a more acute power on the part of the neurologist into the intricacies of his special problem.

The various results of psycho-analysis in different hands; its overenthusiastic supporters, jealous of any who do not conform to the strict rules laid down; its detractors, with their accounts of failure; and the intermediate group, patiently awaiting the light, make final judgment as to its permanent value a difficult matter to decide. Through it, however, much comes to light and many a case opens up to therapeutic possibilities denied to them before.

To summarize in a few words, Janet's conception of hysteria, psychasthenia, and other types of the neuroses is fraught with difficulty, and I do so only to keep this narrative in some kind of orderly succession.

It is interesting to know that Freud and Janet started out from somewhat similar points of view and have arrived at very different conclusions. This common point of departure is the notion of the disassociation of consciousness, the tendency of which is common to the type of neurosis which is called hysteria. There is a second curious point of similarity between these two investigators. Janet has attempted to do with his conception psychasthenia what Freud tried to do with the neuroses—that is, to collect under one head a great many different clinical types and associate them together with a common etiology, and by finding a common psychological mechanism, to consider them finally as slightly different types of one disease condition. Janet calls this psychasthenia, and Freud has done the same with the compulsion neuroses. Janet has assembled together such conditions in which doubt, fear, uncertainty, scrupulosity, etc., are the clinical expressions. In this way he has entirely separated them from dissociation states, etc., as represented chiefly in the hysteric group.

Janet's notion of hysteria best expresses this last idea. That it is a form of mental depression characterized by the retraction of the field of personal consciousness, with a tendency to the dissociation

and emancipation of the system of ideas and function that constitute personality. To this is added the idea that in order that hysteria may be produced in any individual a definite state of depression or exhaustion of the higher cerebral functions is necessary. The lowering of the nervous strength produces in some manner a superficial retraction and an automatic state of depression. Consciousness is no longer able to perform the more complex operations and becomes enfeebled for the time being. It thus becomes readily the subject of suggestive influence of all kinds. The purely localized factor depends upon the additional fact that any function that has remained weak or disturbed is very apt to express itself in various abnormalities or arrested activities because it is the place, so to speak, of least resistance. That is, whether the symptom should show itself in one or another portion of the body or in one or another function depends upon the fact that wherever the activity or mechanism has remained weak or disturbed in that very place the symptoms are expected to become evident. In addition the more complicated a function is the more likely is it to become dissociated. Such functions that were most active at the moment of emotional shock are the ones that are most likely to show the effect of the dissociative process.

These two sets of ideas appear to me to be the most suggestive and stimulating of the Janet psychology, or, at least, those around which, in a clinical way, efforts at understanding the neuroses may best be grouped.

There has been some effort made to point out the similarities of the Janet and Freudian concepts and to suggest that Freud simply elaborated the Janet theory of dissociation with the sexual etiology engrafted upon it. Such efforts are fruitless, it would seem, at least from the point of view of a paper of this kind.

It is easily seen, however, that there is an identical point of view from which both men have chosen to start—that is, that the neuroses in their mechanism at any rate have this in common—the dissociation state of consciousness as a result of traumata with emotional consequences or accompaniments are of prime importance in the phenomena which afterward makes up the disease picture under whatever name we choose to call them.

Of the Babinski theory, which has particular reference to hysteria and to that alone, nothing is to be said here beyond mere reference to the well-known definition that it is a disease the symptoms of which can be caused by suggestion and can be removed by persuasion. This, of course, is a formula, and Babinski evidently regarded it as such, and no more need be said of it than to point out its great value and the fact that it bears the weight of a very great neurological authority.

Without any attempt at elaboration I should like to refer very briefly to an idea which I am not sure should be associated with any

name, though to Adler is commonly attributed the credit of bringing it out. It is the theory of inadequacy. Adler is a representative of one of the secessionistic branches of the Freudian school, one of the earliest I believe to whom the Freudian yoke began to be rather heavy. In the maze of conflicting literary streams I have found it difficult to follow the development of his particular line of thought, so I have taken the liberty of thinking it out somewhat for myself—disclaiming, however, any idea of originality in the effort.

The idea I have in mind is that certain individuals apparently enter their conscious or interpretative existence with a feeling that almost all things that they are called upon to do are inadequately performed by them, or they find themselves inadequate to their performance. This state of mind can and probably does become unconscious, or perhaps after a time ceases to be recognized by the patient at all; but causes the most divergent symptoms, expressing themselves chiefly in an emotional background as states of depression, doubt, fear, etc. It is possible that certain congenital or acquired physical conditions play their part as well, and the struggle to which individuals of this type are naturally exposed furnish, it seems to me, a logical explanation of much that can later be interpreted from the various points of views which were touched upon in the preceding exposition of the theories which were considered.

With these four notions in view, laying aside many others which, for want of time, are not to be touched upon, let us attempt to briefly consider some of their clinical differences and doubtful phases.

*Clinical Difficulties.* Of the Freudian psychology there are three prime obstacles that stand in the way of their more universal use: (1) the uncertain character of what constitutes the essential facts; (2) the ever-changing conception of what is meant by its central idea, sexuality; (3) the technical difficulties which are placed rather arbitrarily, I believe, upon the procedure of psycho-analysis.

The restrictions placed upon the method itself and the material selected for its use are insisted upon with some exactness by the Freudian school, so that it is almost impossible to make use of it in any large clinical or hospital material. A complete psycho-analysis is a matter of many months, and perhaps can never be completed on account of the endless maze into which the psycho-analyst is lead and the necessity which he feels for obtaining as complete a collection of all the Freudian evidence as possible. The question of time, suitability, and patience restricts for purely Freudian investigations two types of the neuroses—hysteria and the compulsion types, the phobia, anxiety states, obsessions, etc.

It is a surprising thing to note how limited the material becomes in the face of the growing complexity of a therapeutic method and the doubtful selection of cases. Hysteria has become a rarity in clinical and private practice in proportion as our appreciation of its psychology has deepened.

For psycho-analytical study there remains, then, the group of compulsion types, and it is in this group that successes are most often met with. What psycho-analysis apparently accomplishes is not just what the Freudians would admit to be the definite goal of this procedure, but rather a curious interacting influence from physician to patient, less, I should say, by the filtering out of this or that feature of a Freudian history, but a more luminous view of the whole process, frequently, I am led to believe, unaffected by the idea of whether a true explanation has been reached or not. The pertinent fact remains in the patient's mind that there is an explanation and not the mystery that before enveloped him and his disease.

The Freudian psychology is a determinate thing, and as such gains immensely in therapeutic force. It goes, rightly or wrongly, to the root of the matter, and the patient soon begins to perceive the notion of the intellectual attack that is being made upon the disease which is tyrannizing over him to his discomfort and unhappiness. The unraveling, let us say, of the anxiety state by discovering that some traumatic experience of the patient's youth or infancy lies embedded in his consciousness dissociated from the proper emotional outlet and inhibited or repressed on account of the negative tonal background, is a great deal more significant to the sufferer, the idea, is, I mean, than is its discovery as a proof of the Freudian concept. It is in this conception in the patient's mind that this thing may be so, together with a realization of the complexity of the maneuvers necessary to arrive at such a conclusion that finally brings him out of the maze of misunderstanding into which he has become enmeshed.

The Freudian school is right in insisting that they are using a procedure of direct psychological determinism, and their opponents are wrong, I think, in asserting that their therapeutic results are gained chiefly by the influence of suggestion.

The cure or improvement of the neuroses is intellectual as is the method used, and the great strength of the Freudian school in my opinion is due chiefly to this fact.

For the neurasthenia I can see no place in the Freudian schedule, that is, if we restrict the term to the definition of fatigue states. Neither the masturbation nor the *coitus interruptus* etiology is convincing enough, nor does it fulfil a sufficient quantitative test to warrant a definite conclusion. These are episodes in many histories, it is true, but the patient remains unconvinced as to their prime importance, and to insist is to suggest, and to suggest is to deny one of the fundamental principles of the Freudian school.

But here, again, comes the great gain which we owe to the Freudian school. The neurasthenic is studied in a way that he never was before and by virtue of the tendency to minute analysis, which should be developed in all serious users of the psycho-analytic procedure, facts, experiences, emotional instances, curious byways in

the patient's life are patiently sought for until a more complete picture is worked out than the patient himself has any idea of. This turning into himself of the patient's scrutiny under the guidance of the psycho-analyst is of the utmost therapeutic importance.

The practical application of some of the Janet principles are less easily demonstrated. They are particularly adapted to rarer types of hysteria. It is a purely suggestive therapy in which hypnosis, or hypnotic procedures, are essential.

But here, too, the role of dissociation of consciousness and the important part played by traumatism in which emotional reactions are common qualities lead to a broader etiological outlook and a more careful search into the past of the patient. Of particular importance, I believe, is the Janet theory in the hysterical affections relating to the complicated mechanism of the special senses, seeing and hearing particularly. Here the dissociation is so obvious that the therapeutic effort at synthesis is unmistakably set out, and whatever the effort may turn out to be, whether of hypnosis, persuasion, reëducation, or training, the positive picture of the mechanism lends a great deal of force to the therapy which is applied.

So, too, in the psychasthenia class, when once we recognize the picture in this sense, we are prepared to give the effort a kind of realism, if I may use the word, which, without this application, would be, I fancy, totally lacking.

The patient's gain is obvious. To the intelligent victim of doubt, hesitation, scrupulosity, etc., a scheme of reasoning about his disease is a source of great comfort, and he feels upon much more certain ground when the mystery is somewhat removed and he can see to what end the therapy is tending.

The clinical application of the Babinski concept is less easily demonstrable, chiefly, I imagine, because it is after all a sort of formula, a kind of definition, and not a very convincing one at that. I should say its chief virtue lies in its prophylactic nature. No one can well doubt that in the realm of the traumatic neuroses it would have a certain application. Here the patient is very suggestible to all kinds of investigative maneuvers, and the neurologist, fortified with the Babinki formula, will attempt to get by with as little unnecessary examination technic as is possible. In such instances, for example, the patient if he be quickly isolated and studied with as little disturbance as possible, and the observation part be carried through with the utmost regard to avoid any element of suggestion, the chances are very good that no suggestive sympton will be developed.

The theory of inadequacy is chiefly illuminating not as a therapeutic procedure, but as lending a sort of understanding of possible protective agencies in a limited class of cases for which no obvious explanation can be found. Here, again, I believe, that the idea involved in this notion is of great practical value in the way of

broadening the horizon of the neurologist and lending a kind of easy plasticity in his approach to a case. This is rather difficult to set down in terms of abstract clinical value. To know about this thing is to give an additional grip upon a very complex clinical problem.

I have selected three instances for mention because they suggest what to me seems the great gain which much of the awakened interest in the neuroses is bringing about:

Case I has reference to a youth, aged about twenty years, with what is commonly called kleptomania.

Case II concerns a young woman, aged twenty-six years, the victim of an obsession.

Case III is concerned with a young man, aged thirty-four years, with what may be described as a contamination neuroses—a mysophobia.

I am sure you will understand that these are not to be regarded as clinical reports in any sense, but are simply very brief accounts to illustrate various methods of therapeutic approach, which, as far as I am concerned, would have been impossible without the work that has been outlined in this paper under the term—the newer concepts of the neuroses.

Case I.—This boy was sent against his will to West Point. The discipline and the military atmosphere grew more and more distasteful to him until it seemed that life there would be unbearable. No way appeared open to him to get out, until he found upon reading a book of regulations that theft was considered a cause for dismissal. Gradually the concept took possession of him that if he were caught either in the act of taking things that were not his or if the things were found in his possession he would be sent away. In his locker some time afterward a variety of useless and valueless things were found—old books, pencils, worn-out shoes, etc., all belonging to his classmates. After investigation his resignation was asked for and he was sent home, a subject for neurological treatment, by the staff physician.

This boy asserted, and truthfully, that he was not aware that he had stolen anything, that he had no use for the things he took, and that he had no memory as to the time or occasion of his acts of theft.

The explanation of the case, that of a wish-fulfilment motive acting automatically and unconsciously proved not on y an adequate explanation, but brought the whole puzzling affair to the critical consideration of the patient. It satisfied the need in his own mind that his disease had a certain logical reason for existence, and with this end accomplished he was released from its influence.

The interpretation here sketched was based upon the use of many of the ideas suggested in this review, the carrying out of which took a long time, and the description of which has no place at the present.

CASE II.—This case has reference to a curious obsession in a young woman which concerned the appearance in her consciousness of the figure of a young man whom she had casually met ten years or more ago. This obsessive fixation became so troublesome that depression, suicidal thoughts, inability to work, and other symptoms were making her life an impossible burden. Her definite assertion, over and over again repeated, that this man was a purely imaginary figure having no reference to the actual living reality for whom she had no interest, seemed at first conclusive evidence that the obsession had no particular logical relation to the effects which were produced. By means of interpretation of dreams it soon became evident that her explanation was a purely defensive procedure, intended to deceive the physician and herself, and that the fact was quite a contrary one. This enabled the problem to be put to her in its real relation, and with that most of the abnormal reactions seemed to disappear.

CASE III.—This case has to do with the fear of contamination by syphilis on the part of the man previously infected, but now having through treatment reached what seemed to be a permanent negative Wassermann stage.

The man, very active in business, could no longer keep his position, a very important one by the way, on account of the fear that he would inflict with syphilis anyone who might touch anything that came in contact with him, such as letters, food, utensils, etc. It was found that the basis of his fear was that his mother would be the victim, and it was for her protection that he automatically withdrew himself from contact with the outside world.

He was sent to the Barnes Hospital, where by psycho-analysis and other methods a rich Freudian picture was gradually evolved, without, I may add, many of the embellishments so insistently demanded by the strict Freudian adherent to this type of neuroses.

This man is just now gradually getting about and is preparing to take up his work with the situation as clear as things of this kind can well be, and with his critical insight into the perplexing problem sharpened to a protective mechanism against the pull of his obsession.

With these three instances in mind I shall ask you to consider some of the conclusions to which the thoughts set down in this paper would naturally lead.

The point of view I have tried to assume is that the four theories here alluded to, and others not touched upon, contain in all probability some aspects of truth, though none contain all the truth. Therefore it is justifiable to pick out and select such as seem of use in the problems which the neuroses imply. The complex nature of the neuroses suggest the idea that no psychological system at present in vogue can explain enough of the total problem to warrant including all our therapeutic efforts at studying them under one head.

It is absurd, therefore, to speak of one as a Freudian, or this, or that, because it is freedom of choice and freedom of effort that is desirable and not the limitation placed upon one by the tyranny of one set of ideas.

There is therefore open to the choice of the investigator or therapeutist of the neuroses the following ideas, some of which are capable of being used in the daily work of the neurologists and those who have occasion to treat the neuroses, and all of which have proved their worth by the test of actual experience.

1. The general admission that a psychologically intricate disease is to be treated by a psychologically planned theory.

2. No psychological system or device contains more than a portion of the truth.

3. Therefore it is justifiable to select as much of the truth out of any one system as seems worth while.

4. Psycho-analysis in the Freudian sense offers at the present time the most promising method of investigating and treating the neuroses.

5. The root notion of the Freudian psychology, that of sexuality, is to be regarded rather in the light of a hypothesis rather than a proved fact. The ideas associated with the terms repression, wish-fulfilment, infantile traumata, dream interpretation among the Freudian concepts are of practical everyday value.

6. As a working theory toward the explanation of hysteria and as providing a method of treatment of certain types of hysteria the Janet theory of dissociation consciousness is useful upon which to base synthetic therapy. In a negative way the Babinski idea of hysteria should constantly be kept in mind. The theory of inadequacy furnishes to the physician a broad scheme of approach to many forms of the neuroses.

These seem to me therefore to furnish a broad general structure upon which ideas of causation and mechanism of the neuroses and direct therapeutic attempts upon the neuroses may be based.

These are things, pragmatically speaking, which the newer concepts of the neuroses have brought to strengthen the hands of the neurological therapeutist.

## PRIMARY MALIGNANT NEOPLASM OF THE LUNG.

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Medical literature has been extensively enriched by published reports on cancer of the lung. Whether this wealth of material is due to a greater efficiency in the domain of diagnosis or whether

pulmonary malignant tumors are on the increase remains at present a much-mooted question.

The difficulty which is encountered in attempting to establish an early clinical diagnosis of primary cancer is well known to the clinician, and is amply emphasized by many observers. This difficulty is probably due to the similarity between such a cancer especially in its earlier course and many other intrathoracic conditions, such as tuberculosis, unresolved pneumonia, pleurisy with effusion, pulmonary lues, and thoracic aneurysm. It is not uncommon even in our present-day knowledge to note in our professional literature, instances where the disease has been entirely overlooked, and the nature of the condition has been revealed only through an autopsy. Thus, Swan[1] reported the history of 6 cases who were sent to Colorado with a diagnosis of pulmonary tuberculosis, and the autopsy disclosed the true nature of conditions, all malignant intrathoracic tumefactions. Bromwell[2] relates a case of primary sarcoma of the lung proved by autopsy, which was previously demonstrated in the clinic as an advanced case of pulmonary tuberculosis, with cavity formations. Henrici[3] speaks of a case shown by autopsy to be a primary cancer of the lung in which the clinical diagnosis was unresolved pneumonia. In this case there was a persistency of high fever, delirium, loss of control of both urinary and anal sphincters, purulent and bloody expectoration associated with dulness in the right upper lobe. Many pneumococci and streptococci were found in the sputum. Tubercle bacilli could not be demonstrated.

My own series of primary cancer consists of 7 cases. Four of these have been verified by autopsy. Another was confirmed by operation. The fact is appreciated that although one cannot be absolutely certain of the diagnosis without a thorough necropsy, still it is fair to assume in the light of our experience in the other cases that clinical diagnosis corroborated by the roentgen-ray is certainly worthy of consideration.

In looking over the 7 cases we are confronted with the fact that 5 of them occurred in the male sex, and in 6 the initial lesion was on the right side. That seems to be the experience of other observers and those who wish to delve into the mystery of the etiology of cancer can certainly find here food for thought. The ages varied from thirty-eight to sixty-five years.

Pain and cough were the first symptoms in 6, while weakness and exhaustion constituted the prime reason that caused the other patient to seek medical advice.

Dyspnea was a very early symptom in all, and although at first it was only marked in some, after physical exertion it invariably

[1] Med. Record, November 15, 1913.
[2] Clinical Studies, Edinburgh, 1909–10, p. 284.
[3] Jour. Med. Research, 1912, p. 395.

became worse, so that later in the disease it actually amounted to orthopnea.

Expectoration was variable: in some very little, in others considerable. Monographs have been written on the sputa in pulmonary cancer, and all kinds of characteristic expectorations have been described. Some have even held that prolonged prune-juice expectoration is characteristic of pulmonary cancer, while the grass-green variety has been designated by others as the characteristic expectoration of pulmonary sarcoma. Those of us who have seen jaundice complicating pneumonia can verify Traube's observations that the grass-green variety is certainly not pathognomonic.

Hemorrhage was very common, and occurred in more or less quantities in 5 of the cases. Tumor cells were never found, although a careful and systematic search was instituted in all instances. We do not put too much faith in the diagnosis of so-called tumor cells, as polymorphous polygonal cells can be found anywhere in the respiratory tract.

Cachexia was a late symptom in all but 1 case. In this particular individual, referred to me by Dr. Battle, it occurred very early, and was associated with a profound anemia of the pernicious type. Sarcoma was our clinical diagnosis, which was corroborated by roentgen-ray examination. Unfortunately no autopsy was permitted by the family.

Fever was present in 3 cases, reaching as high as 105° in one individual. This was accompanied by night-sweats and chills, so that tuberculosis and abscess of the lung were very seriously considered.

Leukocytosis was present in every instance, varying from 10,000 to 20,000 per c.mm. There was nothing to be noted about the differential count, with the exception of the eosinophilia in the case referred by Dr. Battle, in which the diagnosis of sarcoma was sustained.

The above is a cursory summary of the symptoms; although persistence and progressive dyspnea, pain and dry cough out of proportion to the extent of physical signs in the chest, should always arouse suspicion of intrathoracic growths, nevertheless these signs and symptoms may occur in a variety of other respiratory lesions. At the first attempt to portray a clinical picture of pulmonary cancer it seemed an almost hopeless task, but on scrutinizing and studying the records of our cases we found a fairly well-defined syndrome, depending, as Stokes has remarked, on the anatomical disposition of the tumefaction.

Pulmonary cancer can be divided into three main clinical groups:

(*a*) Those originating in the pulmonary tissue, or, more correctly, in the alveoli, occupying more or less the whole lobe or even an entire lung.

(*b*) Those beginning in a larger bronchus and affecting those

adjacent portions of the pulmonary substance which are in the neighborhood of the hilum, involving and spreading from the root to the periphery. These cases, besides showing the symptoms of mediastinal pressure and of overcrowding the intrathoracic area, are accompanied by intense pains and embarrassment of respiration.

(*c*) Cancer, wherein the symptoms are marked by the signs of pleurisy with effusion, so predominant that the underlying cause is actually obscured.

As to the physical evidence, the first named presents a variety of classical signs. Change in percussion is not considered an early manifestation, but if light percussion is used, dulness or flatness will be elicited sooner than reported. Auscultation, however, in contrast to conditions in tuberculosis or pneumonia, will show a diminished breathing. Pleurisy with effusion can be easily excluded by the aspirating needle, and it is certainly suggestive of cancer if increasing dulness accompanied by diminished breathing occurs in the upper and anterior part of the chest. This peculiar combination is due, as a rule, to an obstruction of the bronchus by the tumor, causing an added atelectasis of that portion of the lung fed by the affected bronchus. As the tumor grows, degeneration of various kinds may make its appearance, irregular excavation will come about, and physical signs of percussion and auscultation will naturally change. In one of our cases we had all the signs of a cavity, such as metallic rales associated with tympany amphoric breathing. The diagnosis of tuberculosis and abscess of the lung was seriously entertained, but the absence of tubercle bacilli in the sputum on repeated examinations aroused our suspicions of a cancer. These degenerative processes are nearly always accompanied by night-sweats, high fever, and hemorrhages. Another auscultatory sign of great diagnostic value described by Behier and emphasized by Dr. Isaac Adler was the so-called carnage.[4] This is similar to the sound produced whenever the trachea is partially obstructed, and is heard in all classes of pulmonary cancers. This sign is sometimes noted in bronchitis on account of the plugging of the bronchus by tenacious mucus, but in contradistinction to cancer it is, of course, not persistent.

If the disease has lasted some length of time, demonstrable alterations in the thorax may be observed. There will be an asymmetry of the two halves, either in regard to their dimensions or to the degree of curvature. If the lesion attacks the lower or middle lobe, there will be, as in pneumonia and pleural exudates, divisions in the circumference of these parts; but if the upper lobe is affected, as more frequently happens, there will be an alteration in the thoracic arch. Of the first class the two following cases are somewhat typical.

[4] Adler: Primary Malignant Growths of the Lungs and Bronchi.

CASE I.—The patient, male, aged fifty-three years, was referred to me by Dr. Berlinger, November, 1914, with a history of having had grippe four years before. Since that time he had had frequent coughing spells, with expectorations, particularly in the morning. He was a junk dealer, and consequently inhaled much dust. On June 8, 1914, the patient for the first time expectorated blood; after that he had a number of hemorrhages, and stated that at one time he had coughed up as much as a cupful of blood and pus. He had frequent chilly sensations and afternoon fever. During the last three months he had lost fifteen pounds in weight. His appetite had been poor for six months. He complained of pain in the right side of the chest, in the region of the third and fourth rib, which had gradually been increasing. This pain had become so severe that it caused him to stop work in August, and he had not been able to resume it since. There was no history of tuberculosis or cancer in the family.

To recapitulate the principal complaints we found:

1. Pain in right side of chest.
2. Cough with copious blood expectoration.
3. Weakness and loss of weight.

Physical examination showed a much reduced individual; frequent coughing with expectoration; breath fetid; tongue coated. The glands in the neck were not enlarged. The pupils were equal and reacted promptly. The last phalanges of the fingers were clubbed and enlarged (pneumarthropathy). The pulse was 120. The respiration was 24 to 28; temperature, 99°.

*Lungs.* The anterior upper lobe of the right lung presented complete dulness from the clavicle down to the third intercostal space, and from this point downward the percussion sound was reduced. The same complete dulness existed posteriorly to a level of the sixth dorsal vertebra, and from there on relative dulness down to the base. The vocal fremitus was increased.

Auscultation of the anterior upper lobe showed breathing sound sub-bronchial in character. Posteriorly over the upper area, loud rales and sub-bronchial breathing were noticeable. Below the same conditions existed as anteriorly. Vocal fremitus was normal.

In the left lung only a few slight rales were heard. The heart sound was accelerated, low but clear.

The sputum was mucopurulent and mixed with blood; no tubercle bacilli and no tumor cells were found, but many flat epithelial and red corpuscles; few leukocytes; no hematoidin crystal.

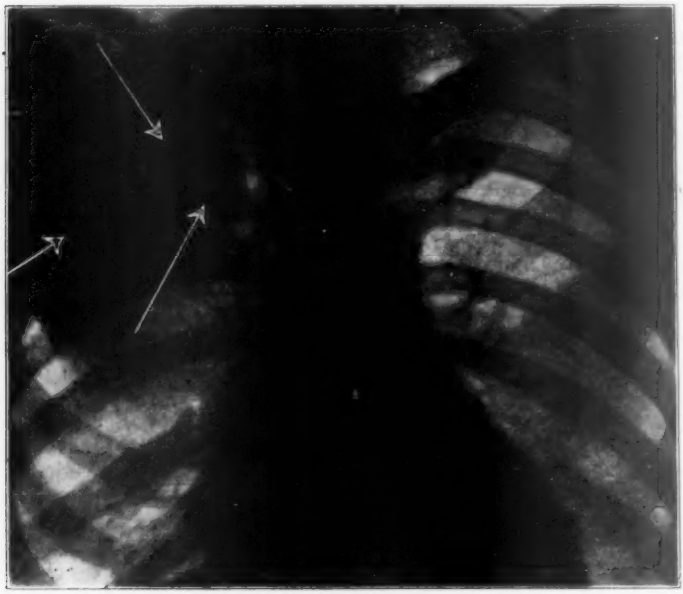
The Wassermann test proved negative.

The urine contained urates and oxalate crystals.

The roentgenogram showed circumscribed shadow in the right upper lobe (see Fig. 1). On repeated examinations the same conditions were found. The temperature mounted higher in the afternoon, ranging from 99° to 105°.

The diagnosis of carcinoma of the lung with degenerative changes in the growth was made. On account of the agonizing pain the patient demanded relief, and was submitted to an operation, on January 23, 1915, at the German Hospital, by Dr. Willy Meyer.

A growth was found at the apex and upper lobe. The tumor had penetrated the pulmonary pleura and had grown diffusely into the surrounding soft parts. The tumor could not be eradicated. The patient stood the operation nicely, but twelve hours later developed pulmonary edema, to which he succumbed.



Case II.—Female, aged thirty-eight years, presented herself at the Polyclinic Hospital, complaining of cough and mucopurulent expectoration. During the last six months the sputum had become blood-tinged. There was neither family history of tuberculosis nor a pretuberculous infection. The pulse was 80, respiration 20, and temperature 98.6°. On inspection there was a dilatation of veins over the chest, more marked on the left side. There was also noted retraction at the left infraclavicular region corresponding to the third intercostal space. The percussion note and respiratory sounds were entirely normal over the right side, but over the left infraclavicular region there was dulness and resistance to finger percussion. The respiratory sounds over this region were faint and expiration somewhat prolonged. Voice and whisper were some-

what distant in sound. Percussion and auscultation of the remaining portion of the left lung were normal.

Because of the above-described signs over the left infraclavicular region, without involving the supraclavicular region of the same side, and because of the normal right side, a tentative diagnosis of tumefaction was made. This was supported by the normal pulse, dilatation of the veins, negative Wassermann reaction, and the absence of tubercle bacilli in the sputum in a number of examinations. Roentgenographic examination by Dr. Quinby at the Polyclinic Hospital revealed a circumscribed mass corresponding to the left infraclavicular region as indicated by the physical signs. The patient was observed for a number of weeks, with but little change in her general strength and physical signs. Since then the patient has not reappeared for examination.

In the second class of primary cancers, those which attack the root and hilum of the lung, a number of symptoms are noted, which are mainly due to pressure on neighboring structures. Closely allied to the resulting symptoms of this type of pulmonary cancer are the signs of thoracic aneurysm, esophageal tumefactions and enlarged mediastinal glands.

Venous obstruction with its picture of dilated veins of the neck, thorax, upper arms, and abdominal walls, associated with edema, is, of course, well known. Particular attention to the venos, azygos major, is paid by Roberts,[5] who cites the case of a boy, wherein at first a diagnosis of acute Bright's disease was made, because of general anasarca, etc., but later, after a more careful examination the effusion in the peritoneal cavity was found to be much less than the effusion into the abdominal walls and lumbar region. This naturally led him to the proper diagnosis, as these parts are drained by the intercostal and lumbar veins, which empty into the azygos major. One of my cases was considered by several clinicians as one of cirrhosis of the liver because of the so-called caput medusa and general abdominal edema. Here the peritoneal edema was quite insignificant as compared to that of the abdominal walls.

Respiratory obstruction by narrowing of the air passages was an early symptom in my cases.

The dyspnea is more intense, especially upon exertion, than in other pulmonary conditions.

Difficult deglutition because of an esophageal pressure is often experienced.

Pressure on the nerves in many instances may cause the first indication, leading the patient to seek medical advice. The nerves which are usually involved are the phrenic, the intercostals, the vagus, or the recurrent laryngeals and the sympathetic; thus irritation of the sympathetic may lead to an exophthalmos, or even more

[5] Lancet, December 21, 1912, p. 1714.

commonly to an inequality of pupils. Pressure on the recurrent laryngeal may lead to paresis of the vocal cords. Although in aneurysm this is a common sequel, affecting the left recurrent laryngeal only, in cancer, both recurrents as a rule are involved.

Pain in this class is extremely intense. The various distributions and intercommunications between the phrenic, the sympathetic, the intercostals, and the cervicals may cause a wide shifting of the referred pain to various localities. The sternum, nape of the neck, and the shoulders represent the most frequent sites. Roberts[6] calls attention to pericarditis as a symptom of mediastinal neoplasm. In my cases there was no sign of pericarditis, but Roberts maintained that pericarditis in the old is as pathognomic of mediastinal cancer as pericarditis in the young is of rheumatism. Besides these symptoms a more or less extensive area of dulness over the lungs must be present. In two of our cases these peculiar phenomena were accompanied by changes in the respiratory sounds. These zones of rapidly changing dulness are due to the atelectasis which is produced and followed by the lung becoming pervious to air again. Of the following 3 cases, which represent this second type of pulmonary cancer, the first will be described in detail. This case has already been reported by Dr. Adler in his monograph on *Tumors of the Lung* and by the author in the *Medical News*.

Case III.—The patient (P. C.), aged fifty-five years, a cigar-maker, gave the following history: No trace of cancer or tuberculosis in the family. He denied lues and venereal infection. Five years previous to coming to our clinic he had experienced pain in the right side of the chest, with unproductive cough. Two years previous to his presentation at the clinic he began to suffer from dyspnea on slight exertion. The pain and the cough became more harassing, and the patient's expectoration became first mucopurulent and finally blood-tinged. On several occasions he had a genuine hemoptysis, with the expectoration of eight ounces or more of pure blood. There was no fever nor night-sweats, nor change in voice. The appetite was good, the bowels were regular, and during the entire course he maintained his normal weight. Physical examination revealed the following:

Fairly well-nourished man, with normal subcutaneous adipose tissue, 5 feet, 5 inches in height, and weighing about 130 pounds. The conjunctivæ were rather pale, and there was slight edema underneath the eyes. Complexion was somewhat livid. No enlarged glands could be felt in the cervical, axillary, epitrochlear, or inguinal regions. Both jugulars were enormously dilated and tortuous. Superficial veins of the chest and upper portion of the abdomen, especially on the right half of the trunk, were also greatly dilated and tortuous, standing out well above the surface of the skin and forming

[6] Loc. cit.

a huge caput medusa. A very slight superficial edema on the right chest was evident. The space above the clavicle was rather full. Respiratory motion was markedly reduced in the right thorax. Careful measurement of the thoracic arch showed no difference in diameter between the right and left side. Apex beat of the heart was not visible, but faintly palpable in normal position. Absolute flatness was found over the whole right chest, extending from the axillary line forward from the clavicle and downward beyond the sternum and emerging over the superficial area of cardiac dulness. Over this area pectoral fremitus was completely absent. The voice was diminished. The breathing was faint, distant, and sub-bronchial in character. There were no rales. On the portion of the lung adjacent to the dulness, expiration was harsh and prolonged. The right lung posteriorly and all of the left lung showed no essential changes. An aspirating needle introduced into the area of dulness seemed to enter solid material. The heart sounds were rather feeble, but there were no murmurs. There was no accentuation of the second pulmonary sound. Heart dulness did not extend beyond the left maxillary line. The radial pulse was fairly soft and regular and of the same volume on both sides. The liver and spleen were not enlarged; no abnormalities could be detected in the abdomen. Reflexes were normal.

The examination of the stomach contents after a test meal showed free hydrochloric acid and the absence of lactic acid. The tube went down with difficulty.

Blood examination made a few days later showed: Hemoglobin, 62 per cent.; red cells, 3,989,000; white cells, 14,000. Differential count gave polynuclears, 54 per cent.; lymphocytes, 34 per cent.; large mononuclears, 8.5 per cent.; eosinophiles, 3.5 per cent.; thus showing a preponderance of lymphocytes and a slight leukocytosis. Red cells stained evenly, but were not equal in size. Microcytes and pear-shaped cells were abundant, but there were no nucleated cells, no poikilocytosis, and no stippling. The repeated examinations of the urine showed no noteworthy change. Temperature was normal, pulse about 80, and respiration at rest 28. Numerous and most searching examinations of the sputum were made. At no time could tubercle bacilli, elastic fibers, or particles of tumor be found. Careful search for actinomyces, streptothrix, and other abnormalities proved negative.

From the facts just stated it seemed evident that we had to deal with some form of neoplasm involving the right chest and the anterior mediastinum, and compressing the large veins, most probably the superior cava. The fact that cough and pain in the right chest had been the first symptoms and had appeared five years before, and the further fact that, according to the patient's repeated statements and assurances, the dilated veins and edema were of comparatively recent date, necessarily led to the assumption of a

primary neoplasm of the right lung that gradually involved in its growth the anterior mediastinum with its contents.

In view of the long duration of the affliction and the comparative state of nutrition of the patient, the slight secondary anemia, the tardy involvement of the lymph nodes, we were inclined rather to exclude the more malignant form of sarcoma and to consider a slow-growing carcinoma or endothelioma of the lung as the most probable form of neoplasm in this case.

The patient and his friends were advised of the unfavorable prognosis, and he was especially warned of a sudden hemorrhage at any time endangering his life.

The patient remained under observation for two months, during which time the disease progressed with great rapidity.

Enlarged lymph nodes appeared first in the right axilla and then in the left, while the cervical and supraclavicular regions remained free. An area of dulness, with harsh and prolonged respiration and diminished vocal fremitus, appeared about the middle of the right lung posteriorly, together with considerable pleuritic friction. Very soon thereafter, with increasing dyspnea and distressing pain and cough, fluid appeared in the right pleural cavity, which rapidly filled.

The chest was aspirated and 20 ounces of clear serous fluid was removed. Almost immediately the pleural sac began to fill up again, but before the patient was ready for another aspiration he was taken in a carriage to a meeting of the medical society, at which he was to be demonstrated by Dr. I. Adler. On the way he was seized with a profuse hemorrhage which ended his life.

An autopsy was performed January 23, 1904, by Dr. Otto Schultze. From a macroscopic examination a tumor mass was found involving the lower end of the trachea on the right side, four rings above the bifurcation, and on the left side just at the bifurcation. This tumor continued and involved the right bronchus, reaching as high as 2 cm. above the origin of the innominate artery. Glands over the anterior portion on the right side of the dome of the pericardial sac were involved in the growth, and the upper lobe of the right lung was adherent to the sac. The growth extended directly through the anterior portion of the lobe of the right lung, following the larger branches of the bronchi to the costal pleura. The rest of the lobe toward the apex was atelectatic and the bronchi filled with pus. The middle lobe of the right lung was the seat of hepatization, very light in color and slightly granular. Wherever the growth pierced the wall of the bronchus to the mucous membrane the membrane presented an ulcerated and eroded appearance. The lower lobe was atelectatic. The diaphragm contained a number of villi markedly injected. The left lung contained a few grayish-white plaques (metastis), 0.5 cm. in diameter, on the posterior surface of lower lobe, on the posterior margin of the base and also on the

surface of the base. Embraced in the mass and constricted by it was the superior vena cava, showing a distinctly puckered arrangement as viewed from the right auricle. The right pulmonary artery showed longitudinal folds with a funnel-shaped narrowing down to the tumor, where the vessel is almost entirely compressed. The heart showed some brown atrophy, but was otherwise normal. The peritoneum was perfectly free. The spleen was small and congested. The liver was normal in size (surface smooth) and pale in color. The stomach and intestines were anemic but otherwise normal. The patient had but one kidney, horseshoe in shape, and ureters passing anteriorly.

The microscopic examination showed a typical flat-celled carcinoma in the primary growth as well as in the metastatic deposits.

CASE IV.—David G., peddler, aged sixty years, complained of dyspnea on slight exertion, pain in the right chest and dry cough, all of which had begun about five years previously. These symptoms gradually became worse, and about two years before his entrance to our clinic his expectoration had already become blood-tinged and his dyspnea had become marked. His family history was negative, with the exception that his wife had died of carcinoma of the uterus. He denied syphilis and his Wassermann reaction was negative. A number of glands in the cervical axillary and epitrochlear regions were palpable and of firm consistency. The jugulars were dilated as well as the superficial veins of the trunk. There was a retraction in the right second intercostal space marked on inspiration. Percussion revealed flatness on the right side of the chest from the clavical downward and from the anterior axillary line inward toward the left merging into the cardiac dulness. Breathing was distant, sub-bronchial in character; fremitus and voice were diminished. The apex was invisible but palpable. The left side of the chest was normal. The heart sounds were feeble but regular. Tuberculin injections of 1, 3 and 7 mg. on respective days produced no reaction. An aspirating needle inserted in the flat area on the right side resulted in dry tapping. The temperature was normal on every occasion. Three months after his first appearance the patient felt decidedly worse, having lost about six pounds in weight and considerable strength. The chest examination showed now in addition to the signs noted previously, flatness at both bases. An aspirating needle now inserted in the eighth intercostal brought forth bloody fluid in considerable quantity. A gland removed from the supraclavicular region showed on microscopic examination a carcinoma. The patient's condition progressed rapidly, and he died shortly from pulmonary edema.

CASE V.—A male, aged thirty-five years, white, referred by Dr. Battle, stated that he had been in perfect health until within four months ago, when he had begun to feel weak and to lose weight and strength. During this period he complained of cough and expec-

toration, which was at first mucous and later at times hemorrhagic. Dyspnea and intense pain localized in the interscapular region became marked. His temperature was 98.6, pulse 84, respiration 24. His skin was lemon tinted. There was considerable dilatation of the superficial veins anteriorly and posteriorly over the thorax. There was no enlargement of the lymphatic glands. Percussion gave flatness over the right chest, extending from the second intercostal to below the third anteriorly, and corresponding to the same posteriorly. The respiratory sounds were distant and bronchial in character; no rales were audible. Over the other parts of the right chest and the left chest nothing abnormal was disclosed. Roentgenographic examination showed a mass corresponding to the outlined area described. Blood examination showed a profound anemia. White cells numbered 12,000, with an 8 per cent. eosinophilia. No tubercle bacilli could be demonstrated. Complement-fixation for lues and actinomycosis was negative. The high eosinophilia, coupled with the apparently rapid course of the disease, impressed upon us that we were dealing with a primary sarcoma rather than a carcinoma.

The third or pleuritic type in my experience is more rapid in its course than the other two. It is extremely acute, and one is markedly impressed by its behavior. Suspicion of these cases is not aroused until recourse is had to several tappings. Aspiration never relieves, and the fluid, which is at first serous, rapidly changes in character through the hemorrhages. If the patient lives long enough it finally becomes chocolate color. Even after the tapping there is no abatement of the cough, dyspnea, expectoration, and general distress. The dislocated heart never returns to its normal condition. Exemplifying this type are the following two cases:

Case VI.—Mrs. D., aged forty-one years, had been perfectly well until four weeks previous to her first consultation. During, this interval of four weeks she complained of pain on her left side, which was intensified on deep breathing. She suffered greatly from cough and difficulty of respiration. She said she had lost ten to twelve pounds during this short period. Her history included the fact that her mother had died of carcinoma of the uterus. Examination showed dulness over the left chest and flatness posteriorly. Breath sounds and fremitus were diminished. The heart was displaced to the right. Dulness reached as high as the fourth rib in the axillary line. On aspiration a serous fluid was obtained. The heart remained displaced to the right even after the tapping. Within three days the whole left side of the chest was flat. Aspiration was again resorted to and the return fluid was bloody. Repeated aspirations had to be performed in the next few weeks because of the difficulty in breathing, and in the later tapping the fluid had changed to a chocolate color. Edema of the lungs set in suddenly, with a fatal termination within five weeks after her first

consultation. Autopsy showed a left pleural cavity containing a considerable amount of chocolate-colored material. The lower lobe consisted of a complete airless, firm white mass. The middle lobe was soft and purulent and on section showed a cylindrical carcinoma. The right lung was edematous and hyperemic, otherwise by no means abnormal.

Case VII.—Woman, aged forty-two years, was seen in consultation with Dr. Morgan. She was the mother of five children and had had typhoid twenty-five years before. Her personal and family history were absolutely negative. The patient stated that eight weeks previous while at dinner an amusing conversation had caused her to laugh excessively and started a cough, which remained unabated for three days, and which was not relieved even by opiates. According to her own knowledge this was the first evidence of cough she had experienced up to that time. Besides her cough, she now complained of weakness and dyspnea.

On physical examination the left chest proved absolutely normal, but at the right base posteriorly there was moderate dulness. Breathing sounds were distant and a few rales were audible. She continued in an unchanged condition, with a slight even temperature, for ten days. Her dyspnea then became intense and physical examination by Dr. Morgan revealed signs of pleural effusion in the right chest. There was cardiac displacement toward the left. The patient was transferred to St. Elizabeth's Hospital, where the dyspnea became exaggerated. Aspiration of the right chest showed bloody fluid. The heart did not return to its normal condition. Signs of pleural effusion returned in the next few days, after the tapping, and during the remainder of her life, which lasted three weeks after her admission to the hospital, several aspirations were performed. No tubercule bacilli or tumor cells were ever in the pleural fluid. The white blood cells count was 15,000. Her temperature during the interval in the hospital varied from 98° to 102°. Autopsy revealed an endothelioma of the base of the right lung with involvement of the right pleura.

In differentiating pulmonary cancer from other conditions, the anatomical distribution must necessarily be taken into account. If the disease attacks the lower lobe it can easily be taken for a simple pleurisy, especially in the early stages of the disease. Exploratory puncture in early carcinomas may be negative. But if a pleural effusion is present the fluid returns after tapping, and soon changes its character from a serous to a bloody or even a chocolate color. Percussion immediately after aspiration will still show in tumor cases a persistence of dulness. Again, as stated before, the heart even after tapping remains displaced in these conditions.

If the tumor occurs in the upper region tuberculosis must be excluded. It is well to suspect cancer in an elderly patient with cough and bloody expectoration if the tubercle bacilli are persistently

absent and the tuberculin tests are constantly negative. Dilatation of the veins and peculiar changing zones of dulness always point strongly to a tumefaction. In cancer you will again find that the dyspnea and the subclavicular pains are distinctly more intense. Again, in tuberculosis we have never seen a case wherein a great amount of tissue was involved on one side in which the other side was not affected to a more or less degree. In contradistinction to this, in primary cancer the other side is comparatively healthy, so that at least the physical signs of infiltration are certainly doubtful or absent. Again, if supraclavicular glands are present, excision should be resorted to and a specimen of the tissue submitted to the microscope.

With regard to aneurysm the roentgen-rays, which are of great service in the diagnosis of cancer, may be of little use in differentiating these two conditions. There are a few instances wherein the tumor lies upon the aorta and gives it an expansile character. It is not uncommon to have a difference in the two pulses in pulmonary cancer because of the subclavion pressure, which naturally adds to the difficulty in differentiation. Lung tumor though, according to A. Frankel, produces a double recurrent paralysis in contradistinction to the left recurrent paralysis which is usually associated with aneurysm. In cancer there is at times a distinct asymmetry of the thorax due to retraction of that side of the chest where the tumor is localized. The tumor, as it grows, frequently involves the pleura, prohibiting a proper expansion of the lungs. Absence of dulness over the lung and absence of any changes in the sputa would speak more for aneurysm or an exclusive mediastinal tumor than it would for a pulmonary cancer. A positive Wassermann reaction would point to aneurysm rather than to cancer. But it is well to remember that cancer and syphilis of the aorta or any part of the body may coexist. The writer has known of such cases of cancer complicated by luetic aortitis. Echinococcus cyst of the lung may be differentiated from cancer by the complement-fixation test. Roentgenography in differentiating these two conditions is of considerable value. Other pulmonary conditions which must be thought of include: infarct, syphilis, dermoid cyst, actinomycosis, chronic abscess and gangrene of the lung.

The roentgen-rays have considerably furthered the diagnosis of tumors of the lung. They are of considerable value in determining the origin and mode of extension. The commonest form seen by roentgenographers occurs in the upper lobe, where they produce an intense uniform shadow. This shadow does not quite reach the apex, and it may be difficult to distinguish it from other forms of infiltration. Other infiltrating growths may extend from either hilus into the lung field often merging with the diaphragm. Here fluoroscopic examinations in various positions will often differentiate these shadows from pleural effusions and tuberculous nodes by the density

and sharp contours. The bronchoscope has also been used as an aid to diagnosis, but its use at the present time is very limited. What the future has in store for this means of differentiation is a question. The treatment must necessarily, if radical, be surgical.

During the last few years intrathoracic surgery with its improved methods of anesthesia has been materially widened, and we feel that the patient suffering from this dreadful malady should at least be given the opportunity of relief by operation.

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## AN INDIVIDUAL QUANTITATIVE DOSAGE OF TUBERCULIN DETERMINED BY THE CUTANEOUS REACTION: ITS EMPLOYMENT IN THE TREATMENT OF SURGICAL TUBERCULOSIS.

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Tuberculin has been used more or less in the therapy of tuberculosis for the past twenty years. Various methods of determining the desirable amount for administration have been employed, some based on the reaction, some on the tolerance, and others on the opsonic index; but with them all there has been no way in which the severity of the reaction to be produced could be accurately controlled. The dosage has been arbitrarily fixed, and accordingly the effect has varied widely.

In all therapeutic measures, one of our ideals is the accurate determination in each individual case of just the quantity of the agent to be used, necessary to produce the desired result.

In 1910 White and Van Norman reported[1] an accurate method of determining, by means of the cutaneous reaction, the correct individual therapeutic dosage of tuberculin for subcutaneous injection This method they base on the varying sensitiveness to tuberculin of the surface cells of individuals with tuberculous lesions. They believe that the beneficial result obtained from the tuberculin is not due to the tolerance induced, but rather to the reaction of the body cells to tuberculin. No attempt is made to produce a tolerance. The individual quantitative dose is determined by the susceptibility of each patient to tuberculin, as shown by the cutaneous reaction. The desired quantity of tuberculin is that amount which will produce the greatest local, focal, and general reaction without producing constitutional symptoms. In this way one is able to use

[1] Arch. Int. Med., October, 1910, vi, 440.

an effective, yet perfectly safe, initial therapeutic dose; the danger of overdosage, common to all of the other numerous methods in vogue today, is abolished. After a careful study of a large number of cases, White and Van Norman show that the quantity of tuberculin required to produce a cutaneous reaction of 4 mm. will, when introduced intradermically, produce an area of redness and swelling at the site of injection 2 to 5 cm. in diameter. This reaction they call the "minimal cutaneous reaction." In addition, they show that this amount of tuberculin is the desired quantity; that is, the amount which will produce the greatest local, focal, and general reaction without constitutional symptoms.

In order to make this arbitrary law applicable, it is absolutely essential to obtain accurately the quantity of tuberculin that will produce the "minimal cutaneous reaction" of 4 mm. In the cases upon which this report is based the technic used in determining the "minimal cutaneous reaction" has been practically that of the originators. As it is necessary to obtain absorption as readily as possible the solution of Old Tuberculin has been used. The flexor surface of the forearm is chosen for the initial skin test, since this allows the part to be kept in a comfortable position until complete absorption of the solution has occurred. The depth to which the scarification is made and its size are very important in order that the reaction may be accurately measured. The diameter of the scarified area should measure 2 mm., and its base should be definitely pink in color. No blood should be drawn. After cleansing the skin with ether two scarifications are made, one about 10 cm. above the other. A definite quantity, 0.01 c.c. of the tuberculin solution to be used, is then applied, by means of an accurately graduated pipette, to the proximal scarification which is used for the test while the distal one acts as a control. The solution is usually absorbed within half an hour, after which a protecting shield is placed over the area. Measurement of the area of redness and swelling is made at the end of forty-eight hours and seventy-two hours. The maximal reaction is usually reached at the end of forty-eight hours.

As many patients give a minimal reaction to 0.01 c.c. of a 1 per cent. solution of tuberculin, this percentage is used for the initial test. If 1 per cent. is found to be high a lower percentage is chosen, and *vice versa*, until that percentage is found which will produce an area of redness and swelling 4 mm. in diameter. This is the "minimal cutaneous reaction" of the patient, and the amount of tuberculin necessary for its production when injected intradermically will produce a local reaction 2 to 5 cm. in diameter. This then is the amount that is used for the therapeutic injections.

The solutions used for obtaining the "minimal cutaneous reaction," and for therapeutic injection, are made by diluting Old Tuberculin with sterile salt solution containing 0.25 per cent. phenol.

A constant volume is used for the therapeutic injections, so that 0.5 c.c. of the solution contains the desired amount of tuberculin. For example, if 0.01 c.c. of a 1 per cent. solution, that is, 0.1 mg. of tuberculin, produces a 4 mm. reaction the solution for that particular case is made, so that 0.5 c.c. contains 0.1 mg. of tuberculin. Fresh solutions are made for each therapeutic injection from stock solutions of higher percentages, which are kept on ice.

The injection is repeated every fourteen days in order that the patient may retain this reaction to tuberculin. As a skin test is equivalent to a therapeutic injection it is better not to repeat the preliminary skin test for four or five days. The therapeutic injection should not be given until seven to ten days after the skin test has been made, for if given at a shorter interval the local reaction is very likely to be much greater than desired. After cleaning the posterior surface of the upper arm with ether the first therapeutic injection is given intradermically, so that by measuring the resultant local reaction the accuracy of the skin test may be checked. As the intradermic injection may cause some pain for the first forty-eight hours, subsequent injections are given subcutaneously, except that every two months the injection is again made into the skin, in order to determine whether or not the patient has changed in sensitiveness. In none of our patients have we found it necessary to change the initial dose after it had been accurately determined.

A child, aged seven years, with marked bilateral cervical adenitis, was under treatment for twenty-one months, during which time the swelling and redness at the site of injection always remained between 3 and 5 cm.

A case of arthritis of the left hip after being treated six months improved and was lost sight of; after seven months he returned with a large abscess in the thigh. His original dose of 0.05 mg. was injected intradermically with a resulting reaction of 3.25 cm., only 1 cm. less than the initial reaction. Injections were not made when the temperature was above 100°.

Since its adoption in 1911 we have used this therapy very generally in surgical tuberculosis, the only contra-indications encountered and observed being a temperature above 100° F., or disease so advanced as to render any type of treatment of questionable value. The major portion of the operative procedures so generally employed formerly has actually been done away with. The earlier experiences were detailed by Cashman,[2] and the present report is submitted in order to record our results since that time. We feel that the results obtained justify us in a distinct feeling of encouragement, with reference to the possibilities in this somewhat dismal field, the more so by reason of the fact that with few exceptions our patients were ambulatory dispensary cases and obviously unable

[2] Am. Jour. Med. Sc., August, 1913, p. 213.

to alter the general conditions governing their mode of living to any great degree. In our cases tuberculin was not used as an absolute specific, but whenever possible in conjunction with the usual dietetic and hygenic measures. Special attention was given to the mouth, teeth, and tonsils in the cases with involvement of the cervical glands. Fluctuating masses were aspirated or incised when necessary. Sinuses were treated locally by dry dressing, application of tincture of iodin, and occasionally curettage. When joints were involved, extension and fixation were used. Operative procedures were limited as much as possible; for instance, excision of the glands of the neck, which formerly was common, has been only an occasional procedure during the last three years. The diagnosis was based on the physical examination, roentgen-ray pictures, negative bacteriological findings in cases with pus not exposed to secondary infection, the clinical history and microscopic examination of tissue removed. In the duration of treatment we were guided by the disappearance of symptoms and signs of activity at the site of the lesion. An attempt was made to continue the treatment for three months after the patient was apparently well and then to continue observation of the case for the succeeding three months. Most of the cases were taken from the dispensary, and unfortunately became irregular in returning for treatment just as soon as the condition improved. For the same reason the question of instituting proper dietetic and hygenic measures was very difficult, and in many cases impossible. As a result the majority of the cases received only the tuberculin and the limited surgical care outlined above.

In the present series there are 40 cases in which the dosage of tuberculin has been worked out by this method. The oldest patient treated was aged fifty-one years and the youngest fifteen months. Eight were below ten years of age, 15 between ten and twenty, 9 between twenty and thirty, 4 between thirty and forty, 1 between forty and fifty, and 1 above fifty. The largest individual dose of tuberculin determined in the series was 0.3 and the smallest 0.005 mg. This wide variation in the dosage corresponds to and emphasizes the wide variation in the sensitiveness of patients to tuberculin; the value in having a method whereby an individual quantitative dose may be obtained is obvious. The longest period of time over which the treatment was continued was twenty-one months in a case with extensve involvement of the glands on both sides of the neck and multiple sinuses. The long duration in this case was due in part to the fact that the patient was very irregular in returning; after the importance of regularity was impressed upon her and treatment could be systematically carried out the sinuses healed, the glands disappeared, and she gained in weight. She was discharged well, and when seen four months later was in good condition.

Over 500 therapeutic injections have been given, and in only one case were any constitutional symptoms observed.

A woman, aged thirty-five years, with marked pulmonary lesions and involvement of the axillary and cervical glands, was running a daily temperature of 99.5° before treatment was started; after the second injection the temperature reached 100.6°, with some headache and malaise. The tuberculin treatment was stopped and the patient subsequently disappeared.

Of the 40 cases herewith reported the greatest number had glandular disease, namely, 19 cases, all with the cervical group affected, 1 case showing evidence of involvement of the axillary group as well. Of the joints, in 6 cases the hip was involved, in 3 the knee, in 1 the ankle, and in 2 the wrist. In 4 cases the vertebræ were affected. The metatarsal bones and the phalanges of the hand were each diseased in 2 cases. The lesion was located once in the greater tuberosity of the humerus; 16 cases were open and 24 were closed.

Nineteen cases sought treatment because of cervical adenitis, 7 of them having sinuses. Of the 19 cases, 12 were discharged as well, 6 were inproved, and 1 unimproved when last seen. By improvement we mean the closure of sinuses, decrease in the size of the glands, gain in weight, and general condition. Of the 6 improved cases, 2 failed to return after receiving six injections, 1 left the city after receiving two injections, and the remaining 3 are still under treatment. In the case classified as unimproved there was extensive bilateral involvement of the glands of the neck; ten injections resulted in marked gain in his general condition, the glands decreasing in size and his weight increasing 9 pounds. He then had an attack of acute tonsillitis, with increased swelling of the glands and return of pain. After the condition had subsided, tonsillectomy was advised, but the boy has not been seen since; in the light of his previous hostory it seems probable that removal of his tonsils and the continued tuberculin treatment would have resulted in great benefit.

A young girl with cervical adenitis submitted on two occasions to excision of the diseased glands. Following this, although dietetic and hygienic measures were used, the condition did not improve, there being, instead, loss of weight and impairment of her health. Finally, after determining the dosage by the "minimal cutaneous reaction," tuberculin was given; in a short time the glands decreased in size and her general condition improved with a gain in weight. She was discharged in excellent condition, weighing more than ever before, and has since remained perfectly well. No surgical procedure whatever was used in this case after she came into our hands. The average number of therapeutic injections given was 10, extending over a period of five months. This record in the treatment of tuberculous adenitis seems to us very gratifying. Numerous instances of striking and undoubted benefit could be cited, though perhaps the preceding case illustrates very well what may be accomplished.

We have had 6 cases of tuberculous arthritis of the hip; 1 case has been discharged as well and is now at work; 3 were improved and 2 unimproved. Of the improved cases, 1 is now under treatment. Another was treated three and one-half months, and the third, two months, when they failed to return. Of the unimproved, 1 received one injection and the other three injections. Of the 4 cases with involvement of the vertebræ, 2 left the hospital slightly improved and 1 without much noticeable improvement. The fourth is now under treatment and is improving. Abscesses were present in all these cases but one, and were either aspirated or drained.

In 3 cases the lesions were situated in the knee. One was discharged with moderate limitation of motion. The remaining 2 improved and were lost sight of. Of 2 cases involving the wrist, 1 is now well. There is limitation in motion, but no pain or swelling, and he has worked daily for the past three months. The second case disappeared after two and one-half months' treatment much improved. Two cases of metatarsal disease are now well.

Three additional cases will serve to show what may be accomplished in disease of the bone and joints. In a case involving the hip there was acute pain and inability to walk. Extension was applied to the leg, followed by fixation with a cast, when he was allowed to go home, returning from time to time for the tuberculin injections. This patient improved markedly and gained in weight, and was discharged four months ago. He is now working daily, and although he is only fairly well-nourished, he reports himself as perfectly well. In a case involving the wrist, with moderate destruction of bone, there was a very satisfactory result after tuberculin injections and fixation. Although the motion in the joint is limited the patient has been working in an office for three months. A case with disease of a metatarsal joint showed no improvement when treated by fixation alone, but when tuberculin therapy was instituted his condition rapidly improved and he is now able to walk comfortably without pain.

In Pott's disease the results have not been as satisfactory; however, in all but one of these cases the disease was well advanced, with the presence of large abscesses.

Throughout our series we have found that the results have varied in inverse ratio to advancement of the disease. Those cases in which abscesses or secondary infections were present showed slower improvement and less satisfactory ultimate results. The best results were obtained when tuberculin treatment was instituted early.

Of the 40 cases treated, 19 have been discharged well, 16 improved, and 5 have been lost sight of, with the condition unimproved. All of the cases which failed to show any improvement were under treatment for a very short time; as they were lost sight of before

any definite effect could be expected, we feel justified in excluding them in estimating our results. Granting this, there are 35 cases in which the treatment was continued over a reasonable period of time; of these, 19 are well and 16 improved. Of the improved cases, 7 are still under treatment. Our results also varied according to the nature of the tissue diseased. Tuberculosis of the soft parts responded more readily than those in which bones or joints were involved.

Of the 28 cases previously reported by Cashman, 11 were discharged as well and 11 improved, the remaining 6 being unclassified Including these 28 cases with out present series the tuberculin dosage has been obtained and the injections made by this method in 68 cases of surgical tuberculosis. Excluding the 11 cases which have been lost sight of we have 57 cases in which the treatment has extended over a reasonable period of time; of these 57 cases, 30 were discharged as well and 27 improved.

A series of 57 cases of surgical tuberculosis, even though they have been carefully followed, is perhaps too small to allow one to draw any definite conclusions. Nevertheless, in working with this number of cases for a period of more than four years one inevitably receives very definite impressions, and we have no hesitation in declaring that the impressions gained by us have been very favorable. As stated above, our operative work in this field has been greatly reduced, and we think replaced by a much improved therapy. We strongly urge a careful unbiased trial of the method upon those men whose work carries them into this field. These cases have been observed and treated in the surgical clinic of the University of Pittsburgh, and the thanks of the writer are due and gladly given numerous colleagues for help and encouragement.

## THE RELATION OF THE RECENT EPIDEMIC OF RESPIRATORY DISEASES IN DENVER TO PULMONARY TUBERCULOSIS.[1]

By James J. Waring, M.D.,
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There have been under my continuous observation since November 1, 1915, 120 patients with pulmonary tuberculosis, of whom 20 were classified as incipient cases, 42 moderately advanced, and 58 far advanced. Of the first class, 2; of the second class, 9; of the third class, 12 contracted the prevailing respiratory infection, epidemic during the past winter.

The 2 incipient cases recovered completely without any sequelæ.

[1] Read before the Medical Society of the City and County of Denver, Colorado.

Of the 9 moderately advanced cases in 3 and of the 12 advanced cases in 5 there resulted an extension of their tuberculosis. Of the moderately advanced cases, 1 exhibited, four weeks after the onset of "la grippe," an albuminuria with granular and cellular casts, which condition was not present before. Of the far-advanced cases 3 present similar urinary findings without there having been previous evidence of renal disease; 1 far-advanced patient with albuminuria progressed favorably for about five days after the onset of his new infection, and then developed complete suppression of urine for thirty-six hours, and death followed in five days. I am satisfied that this new infection precipitated the functional collapse of his kidneys. One case with severe laryngitis and tracheitis now shows a definite tuberculous laryngitis.

This is a brief summary of the cases of tuberculosis complicated by "la grippe" which I have handled in the last three months, with a note of their complications.

The pathological investigations of Cornet, Babes, Evans, Schutz, Prudden and many others long ago demonstrated secondary invaders in the walls of cavities, even in miliary tubercles far removed from the original focus of infection. There followed the isolation and identification of these germs by the method first suggested by Koch, later applied by Kitasato, and now considerably modified and improved, namely, the washing of the sputum and the taking of cultures therefrom. Inoculation of laboratory animals with cultures taken antemortem and postmortem determined their virulence. Finally, the therapeutic test of vaccine therapy and the demonstration of immune bodies in the serum add other chapters to the story of mixed infection.

It is generally accepted that secondary infection in pulmonary tuberculosis does occur, and is serious, in spite of certain negative laboratory evidence, such as the occasional demonstrated avirulence of sputum isolated organisms and the curious anomaly in the field of comparative pathology, namely, that cavity formation is rare in animals with the exception of monkeys.

During or shortly after an attack of "la grippe" the physical examination may reveal apparently an alarming extension of the tuberculous process; however, the amount of damage often cannot be determined until some weeks have elapsed after the onset of the complication. Such a case I saw recently. A young woman returning from a visit home, contracted "la grippe" en route. Physical examination indicated a widespread involvement of the left lung from apex to base front and back and in the upper and middle lobes of the right lung. Two weeks later her chest returned to the condition presented three months previously: moisture in front on the left to the third rib only and half-way to the angle of the scapula behind; on the right, moisture to be heard only in upper lobe and interscapular region behind.

Granted that shortly after a severe attack of "la grippe" a consolidated lung rapidly disintegrates, that a comparatively slight infiltration becomes more extensive, and where a month ago there were slight changes in the breath sounds and fine and medium moist rales, today there are bronchovesicular breathing and large and medium moist rales, and instead of a symptomless, retrograde process, an actively, even rapidly advancing disease with all the evidences of marked constitutional disturbance; granted all these, what are the intimate details of the transformation? What chemically and biologically happens when simple caseation passes into excavation?

In the past year the work of Jobling and Petersen[2] upon the antiferments has thrown much light upon this question, and is worthy of brief consideration. In acute caseous pneumonia a large catarrhal exudate rapidly becomes caseous, with the death of many cells known to contain ferments, and yet no autolysis takes place. Jobling and Petersen contend that secondary infection results in softening because of the entrance of fresh ferments with the new invaders, and because the body fluids necessarily accompanying the new inflammatory condition dilute the ferment inhibiting substance and aid in its removal. They have shown that lipoids containing unsaturated carbon atoms are antitryptic in colloidal solution; that tubercle bacilli and tuberculous caseous material contain such lipoids; that the reluctance of caseous material to solution and absorption is due to the presence of these compounds; that the inhibitory effect of the antiferments is overcome when the unsaturated bonds are oxydized or satisfied with iodin. This work, in addition, gives a rational chemical explanation for the solvent effect of iodin on tuberculous and luetic tissue, and forms the basis, further, for a new theory of the origin of anaphylotoxin.

The organisms chiefly incriminated in this role of secondary invader have been the influenza bacillus, pneumococcus, streptococcus, and Micrococcus catarrhalis. The investigations as to the etiology of the current epidemic of respiratory infection in Chicago by George Mathers[3] would indicate that a hemolytic streptococcus was the causal agent. Williams and Burdick,[4] in Denver, have also demonstrated a streptococcus, and by most instructive work have proved the selective tissue affinity of the organism isolated.

John Ceconi,[5] medical inspector in the Division of Communicable Diseases of the Boston Health Department, has called attention to the great need of research along biological lines in epidemic respiratory diseases. He considers the influenza bacillus the etiological agent in the recent epidemic, although admitting the great difficulty

[2] Jour. Am. Med. Assn., 1914, lxiii, 1930. Jour. Exper. Med., 1914, xix, 251, 383, 459, and 239; ibid., 1914, xx, 321.

[3] Jour. Am. Med. Assn., 1916, lxvi, 30.

[4] Med. Record, 1916, p. 876.

[5] Boston Med. and Surg. Jour., 1916, clxxiv, 423.

in determining finally the causative organism from inoculated plates, upon which may be found more or less numerous colonies of other pathogenic organisms, such as the staphylococcus, streptococcus, and pneumococcus.

Luetscher[6] has not experienced this difficulty. After establishing proper conditions for collection of sputum for examination, he says: "It will be found that in acute conditions remarkable plates will result, and that, as a rule, one organism will be present practically in pure culture." It must be added that Luetscher's work related to non-tuberculous invalids and to non-epidemic infections.

Williams and Burdick[7] isolated a hemolytic streptococcus from the sputa of patients, demonstrated complement-deviation bodies in the serum, and finally inoculated an emulsion of this germ into the ear veins of rabbits. The rabbits killed forty-eight hours later showed definite tracheitis, laryngitis, and bronchitis.

There is not only disagreement over the nature of the recent epidemic, but there are conflicting reports from bacteriologists over the prevalence of certain organisms in the sputum and the relation of these organisms to the attendant respiratory infection—whether that infection be epidemic or non-epidemic in type. For instance, Lord[8] found the influenza bacillus in pure culture in 30 per cent. of his cases of lung infection in the interepidemic period. Luetscher considers the same organism, next to the pneumococcus, one of the most important infectious agents found in pulmonary lesions. "That it is not only present in pandemics and epidemics, but also the cause of approximately 30 per cent. of the pulmonary lesions in interepidemic periods."

Williams and Burdick, in a personal communication, state that during the past two years in over 500 sputum examinations, using human blood-agar as a medium, they have failed to secure a growth of the influenza bacillus in every instance. During this time the bacillus was grown only twice—once from material obtained from the submucosa of a case of atrophic rhinitis and once from a case of Ludwig's angina. They discovered the pneumococcus only nine times. Williams and Burdick classify the *Streptococcus mucosus* as a streptococcus, a classification which is not generally accepted. Hanes,[9] concludes that Schottmuller's *Streptococcus mucosus* is really a variety of pneumococcus. Its cultural characteristics, solubility in solutions of bile salts and its behavior in comparative complement-fixation experiments all support this opinion. Luetscher[10] found the pneumococcus the cause of 62.44 per cent. of all the non-tuberculous infections below the larynx, and together with the influenza bacillus, the cause of 90.94 per cent. of the infections of

[6] Arch. Int. Med., 1915, xvi, 657.
[7] Loc. cit.
[8] Boston Med. and Surg. Jour., 1902, cxlvii, 662; ibid., 1905, cliii, 537 and 574.
[9] Journal of Experimental Medicine, 1914, xix, 38.
[10] Loc. cit.

the bronchi and lungs, 74.96 per cent. of the infections of the larynx and 31.29 per cent. of the infections of the nose, throat, and sinuses.

Cecil,[11] in a bacteriological study of infections of the upper respiratory tract, recognized the streptococcus viridans as the predominant organism in 56.2 per cent. of 89 cases non-epidemic in type.

It appears therefore that Ceconi, in Boston, determined the influenza bacillus to be the cause of the recent epidemic, while Williams and Burdick, in Denver, simultaneously found the influenza bacillus not a single time.

The consumptive is particularly liable to become infected during an epidemic, among other reasons because of mouth-breathing. This habit may have been contracted in childhood from adenoids or in later life from decreased lung capacity, nasal deformity, toxemia, fever, myocardial insufficiency, distorted mediastinum, or acidosis. In this connection it is interesting to note that Yandell Henderson,[12] of Yale, suggests as a test for acidosis the length of time the breath can be held More than once we have all been impressed by the fact that in advanced pulmonary tuberculosis, usually of the fibroid type, the patient is utterly unable to hold the breath. Occasionally a patient will have hyperpnea apparently out of all proportion to the lung involvement. Such a case will almost surely have a marked acidosis, whether this be due to a heart or kidney complication or to simple pulmonary tuberculosis, with or without reference to altitude. We may safely conclude that the tuberculous individual is prone to breathe through the mouth when from exerton there is unconsciously a need for more oxygen. Moreover, there is a manifest tendency to catarrhal inflammation not only of the entire respiratory tract but also throughout the alimentary canal. The consumptive, is in addition, a physical incompetent. The very first symptom of the disease perhaps was exhaustion. Fatigue and susceptibility to infection go hand in hand. An unpublished observation of Wade Oliver, of the Pathological Institute of the Cincinnati General Hospital, quoted by Woolley,[13] is that the blood taken from the veins of patients who were brought to the hospital in a state of fatigue, such, for instance, as following a debauch, is apt to show large numbers of organisms, especially those belonging to the group of hemolytic streptococci. Oliver thinks their source is in the pyorrheic gingivitides from which most of these individuals suffer. As the physical condition of the patients improves the blood becomes sterile. It has been shown, however, that the streptococcus viridans is the organism chiefly responsible in chronic and the hemolyticus in acute infections of gums.

There is good experimental evidence to support the view that the tuberculous patient has a specifically lowered resistance to the

[11] Arch. Int. Med., 1915, xv, 150.
[12] Jour. Am. Med. Assn., 1914, lxiv, 318.
[13] Jour. Lab. and Clin. Med., 1915, i, 45.

streptococcus and staphylococcus. Sakagami[14] reveals the interesting fact that the serum of tuberculous individuals has less bactericidal power on these organisms than normal serum.

Inmates of sanatoria and residents of the outlying districts of the city are less resistant even than the city dwellers. From the very fact of their isolation they lack the benefits of automatic vaccination that comes from frequent exposure or even repeated slight infections. Their position is somewhat similar to that of the Indians in the North Canada woods, to whom influenza and measles are real scourges.

I know of no experiments which have demonstrated by the use of an aerial route of infection that the organism responsible for the recent epidemic has a selective tissue affinity for the respiratory tract. Nevertheless, granted such a portal of entry, the habit of mouth-breathing, permitting the entrance of germs very much as the night hawk scoops in gnats, a susceptibility to catarrhal inflammation, a little exhaustion, perhaps suburban residence and long absence from exposure to the germs of mixed infection, and it is easily understood why the consumptive usually contracts "la grippe."

As a result of this complication I have recorded in the patients under my care 3 cases having a peculiar homogeneous salmon-colored sputum and marked laryngitis and tracheitis. Of these 3, 2 have cleared entirely and are as well now as before their attack. One case presents, one month later, a persistent huskiness with a definite tuberculous infiltrated larynx. It is not for me to take up the relation of simple laryngitis to tuberculous laryngitis. I will confine myself to a quotation from Lockard's[15] book on *Tuberculosis of the Nose and Throat:* "Acute laryngitis in the phthisical rarely induces the accession of local tuberculosis if the attack be promptly combated, but neglected attacks or frequent infection may, under fortuitous condition, lead to infection, or in healed lesions to a recurrence." Robert Levy, of Denver, from the wealth of his experience, has voiced repeatedly the same opinion.

Four cases not previously showing any evidence of kidney degeneration, developed during their illness a persistent albuminuria with granular and cell casts. It has long been noted that the consumptive apparently overcomes his lung trouble to die later of kidney degeneration. At any rate, we have all been impressed by the frequency of albuminuria in the moderately advanced or far-advanced cases, particularly in those who have been overfed for a long time. A patient raising daily two to four ounces of purulent sputum imposes an eliminative burden upon the kidneys which cannot be estimated, but must be very great. Barker[16] has called attention

[14] Lancet, 1916, i, 127.
[15] Lockard: Tuberculosis of Nose and Throat, 1909.
[16] Am. Jour. Med. Sc., 1913, cxlv, 42.

to the fact that the "toxic glomeruler nephropathies are often due to streptococcus toxins. The possibility of the complication should be thought of in every case of streptococcus sore throat, hence the general practitioner can do much in the way of prevention. *Every individual who suffers from sore throat, tonsillitis, or 'bad cold,' with fever, should be put to bed and be kept warm there until the infection is overcome.* Not only would much renal disease be thus avoided, but also many serious disorders of the heart and of the joints." Not only is it possible that the lungs may be infected secondarily by the streptococcus, either sporadically or during an epidemic, but it is extremely probable that the lung thus infected may become a focus for further metastasis to heart or kidneys. Parenthetically it may even be possible for the tuberculous lung to acquire a mixed infection from an abscess at the root of a tooth.

The *Bulletin* issued by the city of Philadelphia Board of Health says: "Don't forget that this disease"—la grippe—"may be complicated by pneumonia. It causes a profound depression upon the body, and is likely to affect the heart and kidneys."

Bonney,[17] in his book, *Pulmonary Tuberculosis and its Complications*, says: "There is ample clinical evidence to substantiate the belief that a prolonged secondary infection, though slight in degree, is sufficient to produce desquamative and degenerative changes in the kidneys of pulmonary invalids." Again, "Irrespective, however, of this consideration it is clearly demonstrated that kidney disturbances are much more common in those cases of pulmonary tuberculosis exhibiting varying degrees of secondary infection."

In the use of vaccines this established deleterious effect of streptococcic toxines upon the kidney must not be forgotton. In fact, the prolonged administration of any vaccine in anything but small doses may not be without considerable harm to the renal parenchyma. Longcope[18] by injecting egg albumen into animals has produced definite histological changes in the kidneys. That any anaphylactic reaction causes renal degeneration is not perhaps a warranted deduction from this work, particularly as it awaits confirmation. Nevertheless it adds one more warning against indiscriminate vaccine therapy.

The work of Travis[19] would indicate that milk proteins as such do not enter the circulation of severe cases of nephritis kept for some time on an almost exclusive milk diet. We do know that there are many cases on record of hypersensitiveness to egg proteins. The urine of patients ingesting many eggs may contain these proteins. Finally the tuberculous individual taking six to nine eggs daily and having a moderate trace of albumin, with many granular and cellular casts in the urine and losing weight, may upon the withdrawal

[17] Pulmonary Tuberculosis and its Complications, 1910.
[18] Jour. Exper. Med., 1913, xviii, 678.
[19] Annual Report of Health Officer of Port of New York, 1916.

of the eggs from his diet show a diminished quantity of albumin, fewer casts, and a corresponding symptomatic improvement.

In the absence of any specific remedy capable of routine administration in the treatment of tuberculosis, our main reliance must consist in making the patient take and assimilate a large, often a very large, amount of nourishment. From the ingestion, however, of twelve raw eggs, 84 grams of protein, one or two quarts of milk, 28 to 56 grams of protein, perhaps 3 or 4 cooked eggs, besides steak or roast beef, 40 to 60 grams of protein, together with a half-pint or more daily of extractives in the form of soup and beef juice, there should be afforded some idea as to the amount of waste nitrogenous matter the kidneys have to eliminate. Many patients compelled to take this amount of food are already laboring under a severe toxemia from the tuberculous process in the lungs, with perhaps an indolent superadded mixed infection. Given a patient so handled for six to twelve months, or longer it is not surprising there should develop an albuminuria coincidentally with an acute streptococcus infection of the upper or lower respiratory passages. I would not go on record as inveighing against forced feeding. It is invaluable at times. I am convinced, however, that a diet with two or three times the normal proteid standard continued for a long time may pave the way for the functional collapse of the kidneys at such critical times as those of acute severe mixed infection.

Time and space do not permit me to enlarge upon another very important phase of this subject—the possibility of damage to the heart. Reduction of the pulmonary vascular bed, toxemia, or distortion of the mediastinum by adhesions or other cause may severely handicap the heart in pulmonary tuberculosis. Certain it is that in acute articular rheumatism, scarlet fever, in fact in any febrile disturbance due to a streptococcic infection or associated with it, the heart may show sooner or later definite signs of myocardial degeneration. If the non-tuberculous individual should be protected against endocarditis and myocarditis when contending with a streptococcic infection, certainly the tuberculous invalid, whether we accept the theory of cardiac hypoplasia of older writers or not, is more than entitled to that same degree of protection.

Babcock[20] says: "The danger to life from such a degenerative process makes prolonged observation of the patient after convalescence from an attack of influenza highly important," and "not only is the function of the organ disturbed in the course of influenza, but signs of cardiac inadequacy may develop a considerable time afterward."

Recognizing early in November that a severe epidemic of "la grippe" was prevalent throughout the country, and feeling keenly my responsibility not only to my own patients but the many of

[20] Osler's System of Medicine, Lea & Febiger, 1913.

Doctor Bonney's under my care, I diligently and repeatedly admonished nearly all of them not to visit the moving-picture houses, the auditorium, the theatre, and other public buildings; to avoid the department stores above all places in doing their Christmas shopping. (As many as 35 to 40 saleswomen were sent home one day from one of the larger department stores of this city, with an estimated morbidity of 50,000 cases of "la grippe" in a population of 250,000.) They were urged, as far as possible, to keep off the street cars. Many were not allowed to go into the shopping district at all. All were forbidden to visit their friends ill with "la grippe," and were told not to receive any visitor with a bad cold or any recently recovered therefrom. Every patient, tuberculous or not, who contracted "la grippe" was promptly put to bed and kept there until every vestige of the acute infection had subsided.

One word on the subject of treatment after the acute stage: Specific treatment is now the vogue—perhaps not so much as a year or two ago, but still much resorted to.

I am inclined to think that one reason why vaccine therapy in mixed infection is so frequently unavailing is that the germs of the mixed infection have become so firmly established—"dug in," so to speak, in the walls of old cavities, large or small—that even though the serum may show a large content of immune bodies they are unable to reach the germs in sufficient concentration to effect their dislodgment. The walls of these old cavities are composed of tough old scar tissue in which tissue destruction and regeneration are at low tide and blood and lymph circulation stagnant. Phagocytic cells penetrate slowly this tissue and must meet the invading germs improperly supported by immune bodies and with their activity limited, perhaps by age and certainly by their environment. The natural resistance of the tissue cell is low at the immediate point of attack. In these cases the invader acquires such resistance to the defensive powers of the host, and the latter such resistance to the harmful effect of the invader that a prolonged condition of infection ensues—what Hans Zinsser calls a "sort of truce without manifestation of disease?" until a repeated infection perhaps carries off the patient.

The great lesson of this recent epidemic is not whether the causative agent, is a streptococcus that does or does not ferment this or that carbohydrate, but that we and our patients are periodically exposed to a malady of great contagiousness, caused this year by a streptococcus, perhaps next year by a pneumococcus. At any rate, the infection is produced by a germ with whose biological characteristics we are for the most part unacquainted. When it becomes apparent that such an epidemic is upon us, stringent prophylactic measures should be instituted, including the isolation of all cases. The causative organism should be identified, following which it is important that its tissue affinity be established and serological

experiments instituted, to the end that we may know, not so much what value may be placed upon curative vaccine therapy but what protection we may expect from prophylactic inoculation. We should know whether general antigrippe inoculation is feasible.

Other organisms must be studied along lines laid down by Cole[21] Dochez[22] and other workers[23 24 25] in the Rockefeller Institute in the case of the pneumococcus and by Martha Wollstein[26] in the case of the influenza bacillus.

In conclusion, in pulmonary tuberculosis "la grippe" may prove a fatal complication—the last straw that breaks the back of his resistance—by establishing in the lungs an ineradicable secondary infection with its attendant dangers—by inflicting upon him that dreaded complication, tuberculous laryngitis, by causing the collapse of already overburdened kidneys or weakened heart.

It is incumbent upon us therefore to protect to the last degree the tuberculous invalid from this epidenic form of respiratory infection.

## ANALYSIS OF THIRTY CASES OF PULMONARY TUBERCULOSIS TREATED BY THE INDUCTION OF AN ARTIFICIAL PNEUMOTHORAX.[1]

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In this paper it is my intention to abstain wholly from details of technic and to present that in which after all we are most interested, the results of treatment.

It need merely be mentioned that by the induction of an artificial pneumothorax it is sought to compress the lung in an "air splint," this air splint consisting of nitrogen gas allowed to flow between the parietal and visceral layers of the pleura; and that by maintenance of this compression and consequent absolute rest to the damaged organ for a period of time varying from six months to three years it is hoped to obtain cicatrization and healing of the diseased lung. Cases suited for this treatment are either those that are wholly unilateral or those with severe involvement on one side and comparatively insignificant disease on the other.

In my work I have used exclusively the puncture method of

[21] New York Med. Jour., 1915, ci, 1 and 59.
[22] Jour. Exper. Med., 1912, xvi, 665.
[23] Dochez and Gillespie: Jour. Am. Med. Assn., 1913, lxi, 727.
[24] Bull: Jour. Exper. Med., 1915, xxii, 457, 466 and 484.
[25] Gay and Chickering: Jour. Exper. Med., 1915, xxi, 389. Chickering: Ibid., 1915, xxii, 248.
[26] Wollstein: Jour. Exper. Med., 1915, xxii, 445.

[1] Chairman's address in the Section on Practice of Medicine, read before the North Carolina Medical Society.

Forlanini, inserting the needle through the different layers of tissues until it was seen by the characteristic negative fluctuations of the water manometer with which the needle was connected that the eye of the latter lay between the pleural layers. With the needle carefully held in this position the manometer was turned off and the gas turned on.

The cases treated by this method have all been advanced cases with the exception of 4. In 3 of these pneumothorax was induced for the purpose of stopping persistant bleeding, and in the

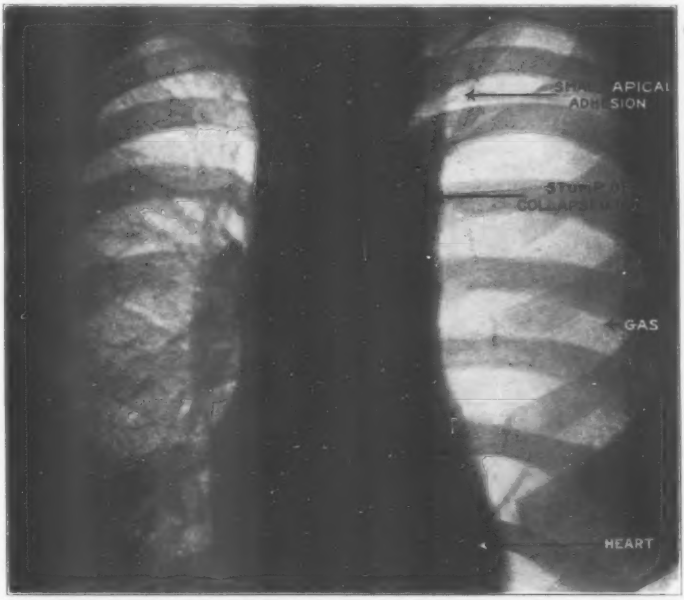


FIG. 1.—Successful left-sided collapse. (Miss A., July, 1913.) Patient well; has resumed household duties; lung has recently been allowed to reëxpand without the onset of any bad symptoms.

fourth case to check a rapid spread of disease from an apparently small focus. Some of the cases have been wholly unilateral; the majority has been bilateral with by far the greater amount of involvement upon the side it was sought to compress.

In the past three and a half years the procedure has been tried in 30 cases. I have grouped my results under five headings:

1. Complete success, 7 cases or 23.3 per cent.
2. Complete success for stopping hemorrhage, 3 cases, or 10 per cent.
3. Partial success (gas still being given), 2 cases, or 6.6 per cent.

4. Prolongation of life for an appreciable period of time, 4 cases, or 13.3 per cent.

5. Failure, 14 cases, or 46.6 per cent.

If headings 1 and 2 are considered together, the percentage of successful attempts is raised to 33.3 per cent.

In the cases coming under heading 1, there resulted a complete cessation of or a very marked diminution in all symptoms. Temperature became normal, cough and sputum disappeared wholly or almost so, and the patients gained strength so that they were

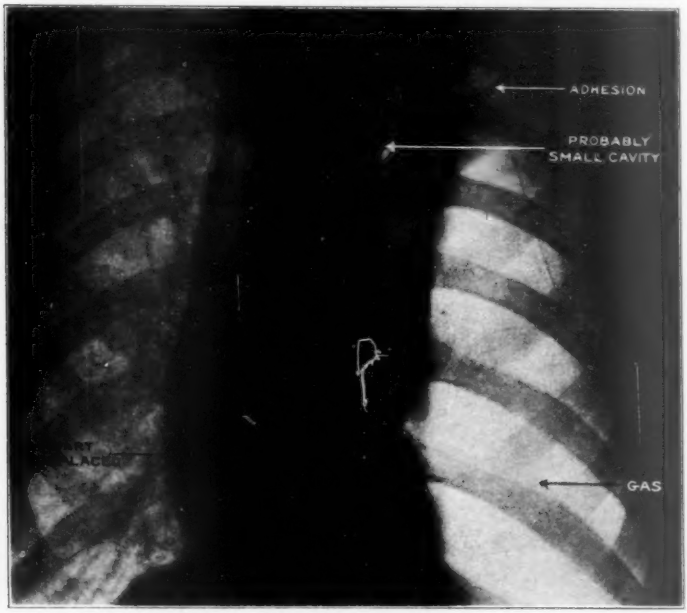


FIG. 2.—Successful left-sided collapse. (Mr. C., July, 1914.) Patient at work. Note marked mottling of sound side and displacement of heart to right of median line.

able to walk without fatigue for an hour or more daily, and were once more able to attend to their household duties or to resume work: in other words, they achieved an "economic recovery." Thus, 1 of these cases (Miss A., Fig. 1) collapsed in July, 1913, is living in the mountain region of Western Carolina attending to her household duties: 1, collapsed in 1914, has returned to teaching; 1, collapsed in 1914, returned to his work of collecting; 1, collapsed in 1914, resumed his studies in Florida; 1, collapsed in March, 1915, resumed her life in Indiana; 1, collapsed in 1914, has taken up the calling of a merchant in Asheville (Fig. 2); and 1 (Mrs. K., Fig. 3)

is still under my care doing very well indeed. These patients have not all stopped taking gas. I know that of the 7 cases 3 are still receiving injections, and perhaps a fourth, unless the effusion which developed on the collapsed side has wholly filled the pleural space. These 7 cases represent the actual saving of 7 lives, for in each case the results of prolonged rest in bed under a strict dietetic-hygienic regimen had born no results, and had it not been for the beneficial effect of collapsing the lung there would have been nothing left to do save to sit by and watch the patient die.

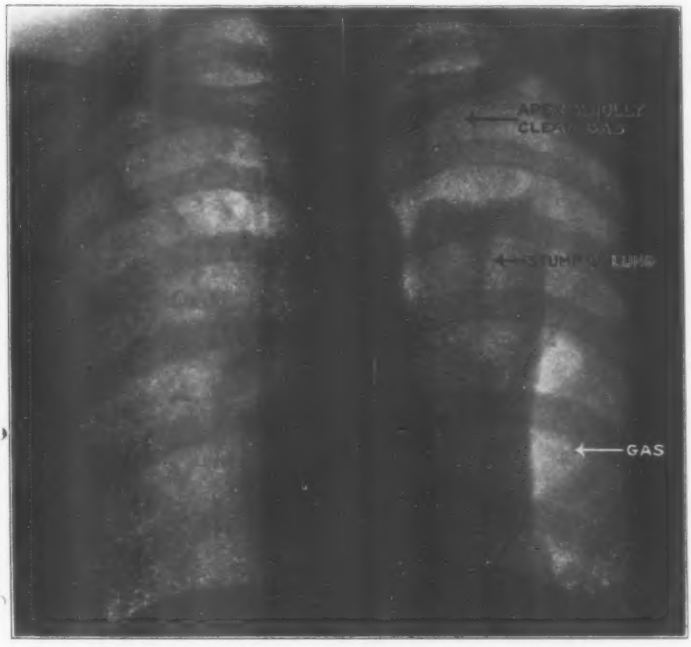


FIG. 3.—Successful left-sided collapse. (Mrs. K., January, 1916.) Lung compressed downward. No apical adhesions.

In my series 4 cases were compressed for the stopping of profuse and continued bleeding, and 3 out of the 4 were successes. In the fourth case the bleeding was stopped, but the patient was so nearly exsanguinated that he could not rally, and death ensued within three days. This case is, therefore, classified under the heading of Failure. The hemorrhage cases are not included under heading 1, because it was not my intention in these cases to continue compression after being certain beyond a reasonable doubt that a firm clot had formed over the site of bleeding. The procedure of compres-

sion was a temporary and an emergency measure. In one of these cases, that of a physician, I had declined to collapse his left lung a year previously because of too great involvement on the right side. I lost sight of him but was called in September, 1914, to find him bleeding profusely from the left lung. Medical measures seemed to have no effect whatsoever. Gas was introduced on the left side and bleeding promptly stopped. The patient was well-nigh exsanguinated, but pulled through with the help of vigorous stimulation. Compression was maintained for two months. He then left, greatly improved, for his home in Virginia, and, I subsequently heard, became well enough to resume a limited amount of his practice. In another case seen in consultation the patient was so exsanguinated as to appear moribund; 3 injections of gas stopped the hemorrhage in this case, and bleeding never recurred. The patient eventually died of his tuberculosis, but lived on many months after the checking of the hemorrhage. Another case was given 3 injections within a week into the left pleural cavity for the purpose of controlling numerous moderate hemorrhages—3 or 4 ounces every four to six hours. Bleeding was checked by the first injection of 900 c c. of gas and wholly suppressed by the second injection of 600 c.c. given thirty-six hours later. The third injection of 600 c.c. was given four days later to ensue no further bleeding as the patient was not readily accessible, being some twenty miles from Asheville. His physician has recently written me that no further bleeding has occurred and that he has made uninterrupted improvement.

Though the number of cases in this class is small, yet the results have been so brilliant that I strongly advocate using gas for checking hemorrhage if severe or protracted, and influenced by medical measures.

I have 2 cases that I have grouped under heading 3: (Miss P., Fig. 3, and Mrs. W., Fig. 4). Both have been under observation for some time: 1 since December, 1914, and 1 since August, 1915. The lives of both have unquestionably been saved by pneumothorax, yet their condition now is by no means one approaching complete recovery. Temperature has been wholly banished in one case (Miss P.) and reduced to a maximum of 99.4° in the other (Mrs. W.), but cough and sputum containing tubercle bacilli continue to an amazing extent, though less so than before the use of gas. Both cases are moderately dyspneic and one (Miss P.) cannot do more than one-half hour's walking without distinct fatigue. Both are holding a rather subnormal weight, which, however, is rather characteristic of gas cases, due probably to a marked deficiency in the blood-oxygenating surface. The reason for the persistence of symptoms in the 2 patients is, as will be seen by consulting the roentgenographs, that an incomplete collapse has been obtained and one or more cavities are held open by pleural adhesions. The walls of the cavities being unable to coaptate, secretion continues,

hence cough and sputum. These patients have reached the limit of possible improvement as far as pneumothorax is concerned, and the gas injections should be continued indefinitely. This is not encouraging in one sense, and yet, on the other hand, there is no reason why both these patients should not enjoy their present state of health for years to come, and that state of health is such as to enable their lives to be by no means devoid of happiness and usefulness.

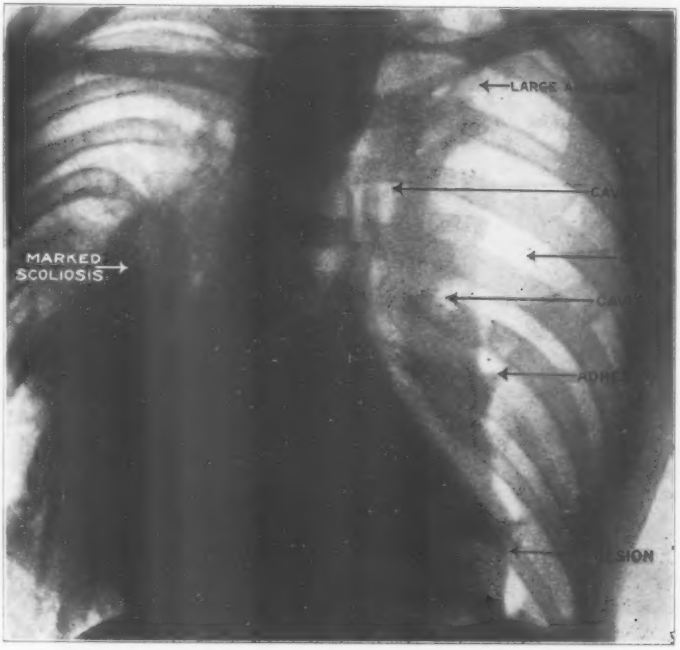


FIG. 4.—(Miss P., December, 1914.) Left-sided collapse; partial success; gas still being continued.

Four cases appear under heading 4. All these patients have died, yet in all the gas alleviated their symptoms to a considerable degree, rendered them more comfortable, and appreciably prolonged their lives. In one case life was unquestionably prolonged for a year; in another for six months; in 2 others for at least four months. Death occurred in 1 case from a sudden dissemination of the tuberculous process in the uncompressed side, with symptoms typical of an acute suffocative phthisis; in 1 from an acute exacerbation of a chronic nephritis; in 1 from the development of a perforation from the pleural cavity into a bronchus with a resulting pyopneu-

mothorax; and in 1 from a gradual creeping spread of the tuberculous process in the uncollapsed lung; gas in these 4 cases was a palliative measure—a help—nothing more.

The last heading, that of Failure, looms large, embracing 14 cases, or 46.6 per cent. of the total number. The number is too great to permit of a detailed analysis of each case, but the following causes for non-success are assignable:

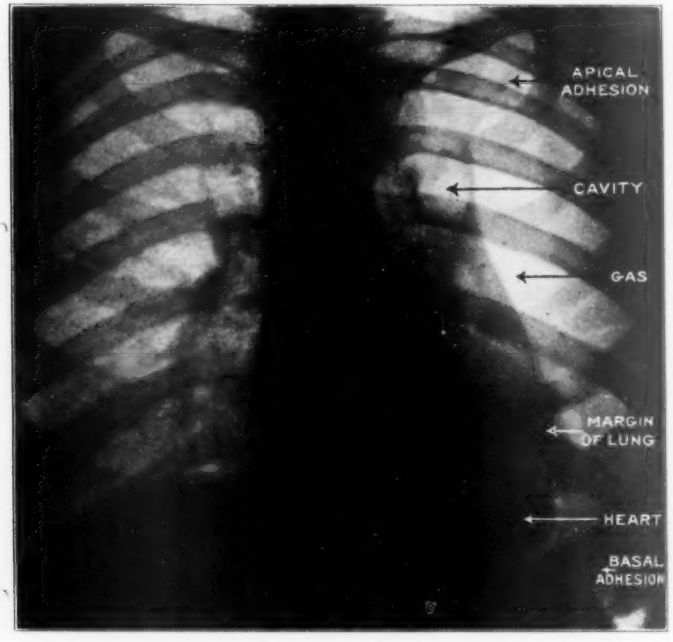


FIG. 5.—(Mrs. R., August, 1915.) Left-sided collapse; partial success; gas still being given.

1. Pocket formation: small amount of gas injected, but surrounding adhesions so dense as to preclude any appreciable amount of collape, 5 cases, or 35.7 per cent.

2. Adhesions so dense as to obliterate pleural space, 5 cases, or 35.7 per cent.

3. Compression obtained to a decided degree, but no result apparent, probably because of deep-seated undiscoverable or undiscovered disease in opposite side, 2 cases, or 14.2 per cent.

4. Development of tuberculous pneumonia in opposite side, 1 case, or 7.1 per cent.

5. Exhaustion: collapse obtained, but patient too near death to rally, 1 case, or 7.1 per cent.

It is thus readily seen that in over 71 per cent. of the failures adhesions were responsible. Adhesions are indeed the one great impediment to the successful beginning of a pneumothorax, and the one great obstacle to its becoming complete when started.

Upon looking over this brief review the conclusion is obvious that the method is worth while and that artificial pneumothax as a factor in pulmonary therapeutics has come to stay. Any method whatsoever that shows success in almost 25 per cent. of the cases cannot and should not be disregarded. In the hands of physicians experienced in lung work and having a full knowledge of the very simple technic and of the possible dangers, accidents due to this procedure should be reduced to a minimum, and many individuals otherwise hopelessly doomed should be restored to complete or comparative health and to many years of joy and usefulness.

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## A CONSIDERATION OF THE CAUSES OF RECURRENT SYMPTOMS AFTER OPERATION FOR GASTRIC AND DUODENAL ULCER.[1]

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The surgical treatment of ulcer of the stomach or duodenum does not terminate with the completion of the healing of the abdominal wound and the discharge of the patient from the hospital. It should properly be followed by a long period of careful after-treatment, extended over months and perhaps years, and directed toward the correction of those accompanying disturbances in the functions of the stomach which are always initiated by the ulcerative process. Such treatment is properly in the domain of the general practitioner from whom such patients are usually referred for operation, or in that of the expert medical man devoting himself to the care of these disorders of the stomach or duodenum. During this postoperative period symptoms frequently arise referable in a general way to the seat of the original trouble, at times at variance with those complained of before operation, at other times mimicking these ante-operative symptoms in some of their aspects, and often

[1] Read at a meeting of the Medical Society of the County of New York. The subject here discussed was assigned by Dr. A. A. Berg, to whom I am indebted for this privilege, as part of a symposium on gastric and duodenal ulcer given from the service of Dr. Berg at Mount Sinai Hospital, New York.

again reproducing with faithful accuracy the original symptom-complex. Much against the usual impression prevalent among medical men these are not always due to the unhealed original lesion, or to its recurrence or to new ulcerations. Much oftener they are caused by other conditions which may be at a distance from the seat of the orignal trouble, or are due to disturbances of the normal physiology of the stomach or duodenum, or are consequent upon the new anatomical relations made at the operation.

For the purpose of pointing out the causes productive of these postoperative symptoms we have made a careful study of all of the patients operated upon for gastric or duodenal ulcer. We have correlated the postoperative complaints of these patients with anatomical and pathological facts made evident at secondary operations and have attempted to show the physiological relationships between the resultant postoperative symptoms and the causative objective findings.

It is essential that one have a clear conception of actual conditions at the time when these patients are discharged from the hospital. The ulceration is not the only condition which the patients have had. Associated lesions are always present which account for many of the symptoms. Anatomical changes in the wall of the stomach are produced by the inflammatory reaction around the ulcer. These lead to hypertrophy or rarely to atrophy of the mucous membrane, with immediate disturbances in the secretory function. Changes in the musculature lead to increased or diminished activity. Frequently mechanical faults in the emptying power of the stomach are added, having been initiated by stenoses of the pylorus or duodenum. The neighboring organs, too, are oftentimes compromised functionally by reflex disturbances and anatomically by adhesions or other abnormalities. Long periods of suffering have gradually brought about a curtailment in the amount of food taken and all of the patients come to operation in a more or less undernourished state.

The methods of surgical treatment which are employed on this service for ulcer of the stomach or duodenum depend naturally on the location of the ulcer and on the presence or absence of associated lesions. The methods are as follows:

1. The ulcer-bearing area is removed by local excision or by resection in continuity of the middle segment of the stomach.

2. The ulcer-bearing area is removed by pylorectomy or partial gastrectomy and a gastro-enterostomy is made.

3. A gastro-enterostomy is made and the ulcer-bearing area is excluded by the string method.

4. In a certain number, for technical reasons, the entire stomach and duodenum are excluded by making a jejunostomy. The patient is then fed through the jejunal tube.

The preparations for these operations, the operations themselves,

and any postoperative complications have all the more intensified the abnormal and undernourished condition present when the patient is first admitted to the hospital. Sufficient time after the operation has not elapsed, owing to the exigencies of hospital economy, for the readjustment to the normal of the accompanying disturbances in the physiology of digestion, and the associated gastritis has not had time to regress and disappear. However, the subjective symptoms have been alleviated and the gnawing pain and the distressing nausea and vomiting have disappeared. The patients believe that a cure has been accomplished and excesses are immediately committed and relatively enormous quantities of food, very often, too, badly prepared food, are taken. What is to be expected immediately happens and gives us the first and perhaps largest group of cases.

Symptoms due to Functional Disturbances. These patients begin to complain immediately after their discharge from the hospital. The most common symptom is vomiting and very soon, if not corrected, pain appears, also pyrosis and gaseous eructations. Inquiry discloses the fact that food is being taken in too large quantities and the passage of the stomach tube reveals an abnormal residue of undigested and foul food detritus. Such a state of affairs was exemplified by one of our patients:

He was a man in the forties who had been operated upon for a perforated ulcer of the duodenum. A gastro-enterostomy had been made and the ulcer-bearing area had been excluded by the string method. Upon his discharge from the hospital he returned immediately to his ordinary diet, which was as follows: Breakfast: cereal, several eggs, several cups of coffee, and several rolls. Dinner: several eggs, fish, rolls, and coffee. Supper: soup, meat, potatoes and other vegetables and tea. It was to be expected that the man would complain. The distress which he had at first was soon augmented by nausea and relieved by frequent vomiting, symptoms which had not been present before operation.

This group of postoperative symptoms, which are the most commonly encountered because the patients are difficult to control after leaving the hospital, are easily relieved by a carefully arranged diet and a systematic course of stomach washings.

Ulcer of the stomach or duodenum is almost always associated with changes in the quality and relative quantities of the ingredients of the gastric juice. In the majority there is an hyperacidity, in the minority an hypoacidity, in a very few an anacidity. It is found that following the operation these changed conditions tend to adjust themselves and return to the normal. In the one case the amount of acid increases and in the other it diminishes. The hyperacidity present before operation may have been of an excessive degree, and it then frequently happens that the postoperative fall has not been sufficient to approximate to the normal and a state

of relative hyperacidity persists. Or it is found that the relative acidity having fallen to the normal level, returns after a short interval again to a hyperacid state. Hand-in-hand with this there is always associated a disturbance in the muscular activities of the stomach, leading to a delayed motility, so that abnormal residues are always found in the stomach.

This disturbed condition of the normal secretory function gives rise to symptoms that appear immediately or very shortly after operation. The great majority of these symptoms originate in indiscretions in diet; very few are due to a relative insufficiency in the size of the stoma. The usual symptoms are pyrosis and belching. Secondary symptoms due to a reflex interference with the motility of the large intestine lead commonly to various degrees of constipation, and in a few cases to diarrhea. With the gradual return of the normal strength of the patient and with ordinary judicious care these disturbances tend to right themselves. These cases form perhaps the second largest group.

The postoperative constipation may be a continuation of a similar condition which had preëxisted before operation and perhaps before the onset of the symptoms referable to the stomach or duodenum. Or it may represent an expression of a general atonic condition in which all of the abdominal viscera take part, produced by the handling of stomach and intestine during the operative procedures. It is difficult sometimes to distinguish between these two, and the test usually lies in the after-treatment. In the latter group the condition tends to improve quickly and spontaneously; in the former the condition is very stubborn and requires attention over a long period of time.

The diarrhea which may appear in a few patients is usually a new symptom and is due to changed physiological conditions in the stomach and small intestine, especially to the changes in the gastric and intestinal juices. It may be very mild and then is cause for little or no complaint. It may occur in periods separated by intervals in which the bowels act normally. In this group it is generally of moderate severity. In very rare instances the bowel evacuations are very profuse and are repeated with great frequency. The prognosis here becomes very grave, and almost always these cases go on to a fatal issue. There is no adequate treatment known for the grave form. In the other two groups the treatment must be directed toward the correction of the abnormally changed secretions of the stomach and small intestine and should be based on competent examinations of stomach contents and bowel evacuations.

Several other conditions giving rise to diarrhea after gastroenterostomy are pointed out by Mathieu and Savignac.[2] These are (1) gastrocolic fistula, (2) incomplete stenosis of the bowel,

[2] Arch. d. Mal. de l'App. Dig., 1913, vii, 541.

and (3) jejunal ulcer. The first and second can usually be diagnosed by the roentgenograph; the third is discussed later in this paper.

Other patients are found who frequently begin to complain even before their discharge from the hospital. The symptoms described are exactly the same which were present before the operation. In contradistinction to the clinical course in the previous groups these symptoms do not tend to right themselves nor do they improve with the ordinary medical means. At varying periods afterward secondary operations may be done, and then it is impossible to find traces of any open ulcerations or of the scars of any healed ulcers, or in fact any other intra-abdominal lesion amenable to surgical treatment. It must be assumed therefore that in these patients there had never been any lesion in the stomach and that the original operation had been unnecessary. It may be stated as axiomatic that in order to cure a patient of the symptoms of ulcer of the stomach an ulcer must first of all be present.[3] [4]

Symptoms due to Anatomical Disturbances. Cases are also found in which pain is experienced for a short time following operation. Usually after a period of medical treatment or sometimes spontaneously improvement occurs and becomes permanent. These symptoms are due to a want of accurate apposition in the suture line of the gastro-enterostomy or remaining after the excision of the ulcer-bearing area, with the development of a granulating area which under proper conditions undergoes healing. In no sense should these granulating areas be taken for the so-called peptic ulcerations.

Perhaps more often than we have believed in the past, post-operative symptoms may also be due to the cutting through of one or more of the unabsorbable sutures which we are accustomed to make use of in at least one of the rows of sutures in closing any wound in the stomach or in uniting stomach to jejunum. The symptoms then persist for a long time and would perhaps tend to a spontaneous disappearance after the offending stitch had been cast off, if it were not for the fact that both doctor and patient become restless and a secondary operation is undertaken, which discloses a piece of thread protruding from the suture line. In one of our patients the same cutting through occurred with the exclusion suture, and when the secondary pylorectomy was made half of the string was found hanging free in a much narrowed pyloric lumen.

True peptic ulcerations appear in the line of the stoma or a short distance therefrom in the jejunum in about 2 per cent. of those patients who have a recurrence of their symptoms. The clinical pictures are very characteristic and are as follows:

[3] Mayo, W. J.: Jour. Am. Med. Assn., 1915, lxiv, 2036.
[4] Moynihan: British Med. Jour., 1912, i, 347.

1. A reproduction of the original symptom-complex occurs within a short time after the operation and the patients believe that the old ulcer has reappeared. Progession may be very rapid and perforation with its consequent peritonitis may quickly arise.

2. The symptoms reappear within a short time after operation and continue much the same as before the operation. Most of the cases are in this second group. Sooner or later, too, most of these come to secondary operations.

3. The symptoms develop slowly and gradually a tumor forms in the upper abdomen. At operation one always finds that a fairly large jejunal ulcer has formed, has undergone subacute perforation, and has become surrounded by a large mass of indurated and adherent intestine and omentum. Such a condition is best treated by jejunostomy.

4. A tumor develops as in group 3. Suppuration occurs within it and the abcess ruptures into an adherent hollow viscus.

In other patients the period of good health extends over a much longer period than that indicated in all the previous groups, and the symptoms begin insidiously and increase slowly. With whatever other manifestation the clinical picture begins, vomiting soon appears and becomes prominent. Disturbances are found in the mechanics of the stomach, and these find their origin ususally in a progressive encroachment upon the lumen of the anastomotic stoma. Whenever the pyloric opening has undergone stenosis from some pathological lesion, or whenever the stomach has been unilaterally occluded, an abetting factor preëxists. We have no means except our own experiences in determining the final caliber of our stomata, and we are in the habit of providing for the expected contraction by making the openings overlarge. Nevertheless in a small percentage contraction occurs regardless of anything we may do. In a certain number, too, exuberant folds of mucous membrane falling across the opening of the stoma act as a valve and prevent the proper emptying of the stomach. Such valve formations sometimes occur much earlier. Occasionally, too, symptoms are produced by Murphy buttons when they do not cut through properly.

These symptoms may also be due to badly selected types of operations, such as some of the pyloroplasties, or to properly chosen but badly executed operations. The last are prolific in the production of kinks and other anatomical abnormalities or in the poor functioning of the anastomatic stoma.

At a secondary operation upon a patient who had developed symptoms some time after a gastro-enterostomy had been made for ulcer it was found that the lowermost part of the stoma had been obliterated by contraction. The opening remaining was very small and was situated rather high on the posterior stomach wall. This accounted for the symptoms and for the abnormal residues found in this patient's stomach.

Symptoms due to Anatomical Disturbances in Neighboring Tissues. A certain number of the symptoms are due to other causes consequent upon our operations. Herniæ in the abdominal scars have often given rise to pain which closely simulates the pain of ulcer. Only when the herniæ are cured do the symptoms disappear. The literature describes several cases in which symptoms were due to chronic forms of ileus, of which the following are examples:

Moynihan.[5] In a patient with an ulcer of the stomach a suture gastro-enterostomy had been made. The postoperative vomiting persisted for one year after operation and then the abdomen was opened again. A hernia of the small intestine was found projecting into the lesser peritoneal cavity, the neck of the hernia being an opening in the transverse mesocolon adjacent to the stoma. The hernia was cured, the symptoms disappeared, and the patient remained well.

W. J. Mayo.[6] An anterior gastro-enterostomy was made with a Murphy button in a man for an ulcer of the pylorus and lesser curvature of the stomach. On the fourteenth day there were signs of intestinal obstruction which lasted for forty-eight hours. On the sixteenth day the button was passed, and therafter the patient was discharged well. At the end of a year the patient returned, complaining of constant pain above the umbilicus. At the operation the jejunum was found twisted on its longitudinal axis and had passed behind the afferent loop. The old gastro-enterostomy was divided and a new retrocolic anastomosis was established. The final result is not given.

In a certain number of patients there seems to be a natural predilection toward the formation of postoperative intra-abdominal adhesions. These may be of moderate degree or may be very extensive. They occur also after operations upon the stomach or duodenum. Sometimes these adhesions result from the reparative peritonitis following localized inflammatory areas around the site of the operation, initiated by soiling during the procedures or by slight leakage thereafter. The resulting discomfort bears no relation, mathematically, to the extent of the adhesive peritonitis, but in a certain number the symptoms are apt to be referred to the stomach or duodenum. Sometimes in the course of time these symptoms disappear spontaneously. On the other hand, secondary operations may be found necessary either for persistent pain or vomiting or for acute or chronic obstructions.

Lesions in organs neighboring to or at a distance from the stomach or duodenum are occasionally found to give rise to symptoms which closely resemble those described before operation. The interval of good health may be several months or many years. This is

[5] Duodenal Ulcer, London, 1912.

[6] Ann. Surg., 1902, xxxvi, 243.

especially apt to occur with lesions in the appendix and with cholelithiasis. Moynihan describes such a case:

At the primary operation, which was for duodenal ulcer, stones were felt in the gall-bladder and for an unexplained reason these were left undisturbed. Following the operation the pain returned almost immediately and the abdomen was reopened again and a cholecystectomy was performed. The symptoms then disappeared. Such a history tends to question the validity of the original diagnosis.[7]

Other conditions which may give rise to symptoms referable to the stomach or duodenum are lesions in the spinal cord, especially tabes dorsalis and tumors. Patients are known to have been operated upon for gastric or duodenal ulcer who have later developed true gastric crises, the manifestations of which were referred for a time to the stomach and not to the spinal cord.

In the accompanying table it has been attempted to show statistically the pathological lesions which were found at secondary operations. The table includes cases from the literature and cases operated upon on Dr. Berg's service at Mount Sinai Hospital.

| | Mount Sinai cases. | Cases from literature. |
|---|---|---|
| Contracted pyloroplasty | .. | 2 |
| Contracted or closed stoma | 5 | 3 |
| Induration at stoma | 2 | |
| Murphy button | .. | 3 |
| Peripyloric adhesions | 1 | 1 |
| Adhesions | .. | 3 |
| Kink of afferent loop | .. | 1 |
| Internal hernia | .. | 3 |
| Healed ulcer | 1 | |
| No ulcer | 2 | 2 |
| Cholelithiasis | .. | 1 |
| Suture ulcer | 2 | |
| Gastrojejunal ulcer | 2 | |
| Open ulcer and contracted stoma | 1 | |
| New ulcer | 1 | 3 |
| Open ulcer at old site | 5 | |

The cases quoted from the literature are from case reports in the papers of Moynihan,[8] Munro,[9] W. J. Mayo[10], Noetzel.[11] Kocher,[12] Kelling,[13] Deaver,[14] Clairmont,[15] and Lieblein.[16] The tabel does not include the cases of gastro-jejunal ulcer described in the papers of Van Roojem[17] and Schwartz[18], nor those in the referate of Lublein.[19]

[7] Moynihan: Loc. cit.
[8] Med.-Chir. Trans., London, 1906, p. 471.
[9] Tr. Cong. Am. Phys. and Surg., 1907.
[10] Loc. cit.
[11] Deutsch. Chirurgen-Kongress, 1906, i, 87.
[12] Ibid., 1906, i, 80.
[13] Ibid., 1906, i, 78.
[14] Ann. Surg., Philadelphia, 1908, xlvii, 894.
[15] Mitt. a. d. Grenzgeb. d. Med. u. Chir., 1909, xx, 330.
[16] Ibid., 1910, xxi, 842.
[17] Arch. f. klin. Chir., 1910, xci, 380.
[18] Ibid., 1914, civ, 694.
[19] Centralbl. f. d. Grenzgeb. d. Med. u. Chir., Ref., 1915, xix, 64.

*Recurrent Ulcer.* In discussing those postoperative symptoms due to a recurrence of the ulcerative lesions[20] only a few of the points will be mentioned. There are several factors to be considered:

1. The healing of the original ulcer.
2. The recurrence of the original ulcer.
3. The occurrence of new ulcerations.

It is not known which factor, preëxistent before operation, has been remedied or removed by any of the approved methods of operation. We simply know the crude fact that under proper postoperative medical care healing takes place afterward. What we are cognizant of are certain factors which are capable of delaying the healing of the ulcer. Clinically we know that tuberculosis and syphilis exert this delaying effect on all other diseased conditions, and especially on ulcerations on any of the body surfaces. Ulcers of the stomach and duodenum are no exceptions. The effect is produced most often by the toxic influences of a constitutional disturbance, or rarely it is due to local disturbance produced by the growth of tubercle or gumma within the confines of the ulcer. In the postoperative care of these patients these factors must all be reckoned with if a complete cure is to be expected.

Experimentally the work of Silberman,[21] Litthauer[22] and especially that of Creacimone and Anglesio[23] have shown that in animals the production of severe anemias is capable of prolonging the healing of defects much beyond the normal time. Many of our patients are anemic, quite a few profoundly anemic, and these experimental studies point out the necessity of correcting any such condition which may be present.

As regards the recurrence of the ulcerations or the formation of new ulcerations one may say very little for we are as little enlightened in this respect as in the etiology of the original ulcer. One point, however, should be brought out. A certain number are due primarily to infections with bacteria. The reliability of the work of Rosenow[24] and others showing that the portals of entry are frequently the teeth and the tonsils and that a selective localization of these bacteria occur in the stomach has not yet been firmly established. However, we have experiences described by Bolton[25] in which an exacerbation or a recurrence of symptoms had occurred in the course of a medical cure for gastric ulcer which followed a fresh attack of tonsillitis or an increase or reappearance of pyorrhea about the teeth. Many of our patients as we see them clinically,

[20] This subject was discussed in great detail by Dr. A. A. Berg at the symposium at which this paper was presented.
[21] Deutsch. med. Wchnschr., 1886, xxix, 497.
[22] Virchows Arch. f. path. Anat., 1909, cxcv, 317.
[23] Riforma Medica, Naples, 1914, xxx, 1289.
[24] Jour. Infect. Dis., 1915, xviii, 219; Jour. Am. Med. Assn., 1915, lxv, 1687.
[25] Ulcers of the Stomach, London, 1913.

exhibit a most deplorable condition of the teeth. Certainly in view of these experiences these conditions should be corrected.

A symptom-complex has been described by Eppinger and Hess[26] under the term vagotonia. Frequently these simulate accurately the picture of gastric or duodenal ulcer. It is quite within bound that the continued irritation of an old chronic ulcer may give rise to anatomical or functional disturbances of the vagi nerves. With the removal of the cause, however, one should expect that these disturbances would disappear.

In dealing with recurrent symptoms after operation for gastric or duodenal ulcer, all of these factors must be considered in correctly interpreting the clinical picture. Not always is it a matter of ease; frequently it is only decided at secondary operations which are always more or less in the nature of abdominal explorations.

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## A STUDY OF THE SIGNIFICANCE OF HEREDITY AND INFECTION IN DIABETES MELLITUS.[1]

By John R. Williams, M.D.,
ROCHESTER, N. Y.

Allen, of the Rockefeller Institute, is of the opinion that diabetes is to be looked upon as a functional disturbance rather than as a disease in those organs which have to do with the metabolism of food. Clinical experience, in a measure, tends to support this view. So far as the writer has been able to learn, nomadic tribes and peoples living in a primitive state rarely if ever have diabetes; likewise other degenerative diseases, as arteriosclerosis, cancer, and disorders due to chemical and bacterial intoxications, are quite unknown. It would seem therefore that diabetes is a product of civilization. This phase of the problem, so far as the writer is aware, has never been carefully investigated. If such a thing were possible it would be interesting to study and plot mathematically all of the facts and forces which have played upon the body of the diabetic from the moment of his birth to the beginning of the disease and to correlate with these similar data with reference to his ancestors.

If it were possible to do this one might then be able to determine the influence of heredity, the various infections, chemical intoxications, etc., in the production of diabetes. To one or more of these agencies, at some time or other, has the cause of diabetes been ascribed. Making due allowance for inaccuracy of diagnosis

[26] Ztschr. f. klin. Med. 1910, lxviii, 67.

[1] Oration in Medicine read before the Vermont State Medical Society.

in former years and for better methods of study now in use, one can scarcely fail to be impressed with the simultaneous increase in all degenerative diseases during the past thirty years. In the city of Rochester the comparative death rate from the most common diseases of degeneration is strikingly shown in the following tabulation:

DEATH-RATE PER 100,000 POPULATION.[2]

| | 1884. | 1894. | 1904. | 1914. |
|---|---|---|---|---|
| Apoplexy | 39.2 | 66.8 | 78.9 | 96.7 |
| Cancer | 49.9 | 24.3 | 80.5 | 108.5 |
| Nephritis | 55.8 | 62.1 | 101.6 | 107.7 |
| Diabetes | 2.9 | 7.4 | 16.2 | 17.1 |

These figures at least suggest that there is some factor common to these diseases.

The relation of heredity to diabetes has not been satisfactorily answered. In his recent book, Joslin[3] reviews the subject and concludes that heredity will appear more prominently in the case reports as time goes on, which he suggests may only reflect greater accuracy in vital statistics. He cites and confirms the experience of Naunyn that the more carefully he inquired into the family history the more commonly he found heredity to be present. This has been the writer's experience. Joslin thinks that the importance of heredity may be exaggerated by the fact that while diabetics are likely to know of diabetic relatives, non-diabetic patients give it little thought. He quotes the figures of Heiberg, who examined the family histories of 100 non-diabetics and found only 7 who had diabetic relatives, whereas 100 diabetics had eighteen relatives similarly affected. In 500 consecutive histories of non-diabetic patients, Joslin found only 25 relatives with the disease. It is questionable whether the problem can be fairly approached in this way. Many patients, both diabetic and non-diabetic, cannot account for the medical histories of their relatives. Furthermore, in the experience of the writer it is not enough to merely ask if any relative has had diabetes. The specific nature of the illness, the tenure of life, and the cause of death of each member of the family should be sought and only such histories accepted for study as afford a reasonable amount of data.

With this plan in mind the writer began about two years ago to gather information of this character and, from the records of several hundred individuals, he has selected the case histories of 100 diabetics for comparison with 100 non-diabetics. In but very few of these was it possible to get full data regarding all of the relatives, but none were used in which information regarding parents, grandparents, and brothers and sisters was not fairly complete and reliable. In this selection of cases completeness of data alone was considered. The occurrence of the most common degenerative diseases, arteriosclerosis, diabetes, cancer, and obesity,

[2] Data by George W. Goler, Health Officer, Rochester, N. Y.

[3] Joslin: Treatment of Diabetes Mellitus, Philadelphia, Lea & Febiger, 1916.

TABLE I.—SHOWING THE OCCURRENCE OF DIABETES, OBESITY, ARTERIOSCLEROSIS, AND CANCER IN THE PARENTS, GRANDPARENTS AND OTHER COLLATERAL RELATIVES OF 100 DIABETICS.

| No. of patients. | Diseases. | Parents: Father. | Parents: Mother. | Grandparents: Paternal. | Grandparents: Maternal. | Collateral: Paternal. | Collateral: Maternal. | Familial. | Children. | Total occurrence. |
|---|---|---|---|---|---|---|---|---|---|---|
| 17 | Diabetes only | 1 | 3 | 1 | 2 | 3 | 9 | 7 | 1 | 27 |
| 31 | Diabetes combined with arteriosclerosis, obesity, or cancer | 3 | 7 | 1 | 7 | 7 | 16 | 13 | 4 | 58 |
| Total 48 | | 4 | 10 | 2 | 9 | 10 | 25 | 20 | 5 | 85 |
| 11 | Arteriosclerosis only | 6 | 3 | 1 | 2 | 4 | 3 | 0 | 0 | 19 |
| 30 | Arteriosclerosis combined with diabetes, obesity, or cancer | 10 | 6 | 8 | 7 | 13 | 2 | 7 | 0 | 53 |
| Total 41 | | 16 | 9 | 9 | 9 | 17 | 5 | 7 | 0 | 72 |
| 2 | Cancer only | 0 | 1 | 0 | 1 | 0 | 1 | 0 | 0 | 3 |
| 24 | Cancer combined with diabetes, arteriosclerosis, or obesity | 2 | 8 | 5 | 4 | 2 | 5 | 3 | 0 | 29 |
| Total 26 | | 2 | 9 | 5 | 5 | 2 | 6 | 3 | 0 | 32 |
| | Obesity | All maternal relations in 9 cases; all paternal relations in 1 case. | | | | | | | | |
| Total 15 | Obesity combined with diabetes, arteriosclerosis, or cancer | 0 | 3 | 1 | 2 | 3 | 0 | 5 | 0 | 32 |
| | Total cases with family histories free from diabetes, arteriosclerosis, obesity, etc. | | | | | | 24 | | | |
| | Total cases with family histories of diabetes, arteriosclerosis, obesity, etc. | | | | | | 76 | | | |
| | Total | | | | | | 100 | | | |

were noted. It was assumed that if an individual before the age of seventy-five had a "stroke" or "sudden paralysis" or "dropsy" coming on after middle life in the absence of acute infection he had a sclerotic disease. This test was applied alike to both diabetic and non-diabetic groups. The data were so tabulated as to show differentially the occurrence of diabetes alone and in association with arterial disease, obesity, and cancer in the parents, paternal and maternal grandparents and collateral relatives (uncles and aunts and their children), and among the brothers and sisters (familial) and children of the patient.

These data in the case of the 100 diabetic patients are detailed in Table I, and for purposes of easy interpretation are summarized under the heading Summary of Table I.

SUMMARY OF TABLE I, SHOWING FAMILY HISTORIES OF 100 CASES OF DIABETES.

| | |
|---|---|
| Cases in which no family histories of diabetes, arteriosclerosis, cancer, or obesity was obtained | 24 |
| Cases with family history of diabetes, arteriosclerosis, cancer, or obesity | 76 |
| Total | 100 |

Seventy-six diabetic patients had:

| | |
|---|---|
| 85 diabetic relatives. | |
| 72 arteriosclerotic relatives. | |
| 25 obese relatives. | |
| 32 cancer relatives. | |
| 16 nerve, mental relatives. | |
| Total | 230 |

An examination of these tables shows most convincingly that diabetes, arterial disease, and obesity occur with extraordinary frequency in the parents and ancestors of diabetics, and also that they appear commonly in their progeny. That the phenomena observed in the diabetic group is unusual and not so characteristic of other groups of patients is shown by Table II and its summary, in which are exhibited data similarly gathered from 100 non-diabetic adults composed chiefly of individuals suffering from gastro-intestinal disturbances and a smaller number afflicted with cardiac, renal, and liver disease and minor disorders (Table II).

In the diabetic group, 48 patients had eighty-five either direct or collateral diabetic relatives, whereas in the non-diabetic group only 6 patients had eight diabetic relatives. In the diabetic group, six fathers and paternal grandparents and nineteen mothers and maternal grandparents had the disease. In the non-diabetic group only one father and maternal grandparent had diabetes. Indeed, the family histories of some non-diabetic cases strongly suggest that sooner or later they will become afflicted with the disease. Since diabetes is a disease which usually occurs well along in adult life, to minimize error only adult cases are considered in the non-diabetic group. Attention is directed to the preponderance of

TABLE II.—SHOWING THE OCCURRENCE OF DIABETES, ARTERIOSCLEROSIS, CANCER, AND OBESITY IN THE PARENTS, GRANDPARENTS, AND OTHER COLLATERAL RELATIVES OF 100 ADULT PERSONS ILL FROM SOME OTHER CAUSE THAN DIABETES.

| No. of patients. | Diseases. | Parents: Father. | Parents: Mother. | Grandparents: Paternal. | Grandparents: Maternal. | Collateral: Paternal. | Collateral: Maternal. | Familial. | Children. | Total occurrence. |
|---|---|---|---|---|---|---|---|---|---|---|
| | Diabetes only | 1 | 0 | 0 | 0 | 0 | 2 | 1 | 0 | 4 |
| 3 | Diabetes combined with arteriosclerosis, | | | | | | | | | |
| 3 | obesity, or cancer | 0 | 1 | 0 | 1 | 1 | 0 | 1 | 0 | 4 |
| Total 6 | | 1 | 1 | 0 | 1 | 1 | 2 | 2 | 0 | 8 |
| 17 | Arteriosclerosis only | 5 | 2 | 4 | 8 | 4 | 3 | 4 | 0 | 30 |
| 21 | Arteriosclerosis combined with diabetes, | | | | | | | | | |
| | obesity, or cancer | 5 | 5 | 3 | 3 | 2 | 7 | 1 | 0 | 26 |
| Total 38 | | 10 | 7 | 7 | 11 | 6 | 10 | 5 | 0 | 56 |
| 15 | Cancer only | 3 | 4 | 0 | 3 | 2 | 4 | 2 | 0 | 18 |
| 19 | Cancer combined with arteriosclerosis, | | | | | | | | | |
| | obesity, or diabetes | 4 | 1 | 0 | 1 | 3 | 6 | 0 | 0 | 15 |
| Total 34 | | 7 | 5 | 0 | 4 | 5 | 10 | 2 | 0 | 33 |
| 2 | Obesity only | 2 | 1 | 0 | 0 | 1 | 2 | 2 | 0 | 8 |
| 4 | Obesity combined with diabetes and | | | | | | | | | |
| | arteriosclerosis | 1 | 1 | 1 | 0 | 0 | 3 | | 0 | 8 |
| 2 | | All maternal relatives obese in 2 cases. | | | | | | | | |
| Total 8 | | 3 | 2 | 1 | 0 | 1 | 5 | 4 | 0 | 16 |

diabetic relatives on the maternal side, although it is quite generally believed that the disease occurs more commonly in males than in females. In the writer's series of 175 cases there were 96 males and 79 females.

SUMMARY OF TABLE II, SHOWING FAMILY HISTORIES OF 100 CASES OF ILLNESS OTHER THAN DIABETES.

| | |
|---|---|
| Cases in which no family history of diabetes, arteriosclerosis, cancer, or obesity was obtained | 47 |
| Cases with family history of diabetes, arteriosclerosis, cancer, or obesity | 53 |
| Total | 100 |

Fifty-three non-diabetic patients had:

| | |
|---|---|
| 6 diabetic relatives. | |
| 38 arteriosclerotic relatives. | |
| 34 cancer relatives. | |
| 8 obese relatives. | |
| 8 nerve, mental relatives. | |
| Total | 94 |

TABLE III.—48 CASES OUT OF 100 DIABETIC PATIENTS HAD 85 DIABETIC RELATIVES AS FOLLOWS:

| Paternal. | | Maternal. | |
|---|---|---|---|
| Fathers | 4 | Mothers | 10 |
| Grandparents | 2 | Grandparents | 9 |
| Collateral | 10 | Collateral | 25 |
| Total | 16 | Total | 44 |
| Brothers and sisters | 20 | Children | 5 |

TABLE IV.—6 CASES OUT OF 100 NON-DIABETIC PATIENTS HAD 8 DIABETIC RELATIVES AS FOLLOWS:

| Paternal | | Maternal. | |
|---|---|---|---|
| Fathers | 1 | Mothers | 1 |
| Grandparents | 0 | Grandparents | 1 |
| Collateral | 1 | Collateral | 2 |
| Total | 2 | Total | 4 |
| Brothers and sisters | 2 | Children | 0 |

Equally interesting are the data regarding arterial disease. In the diabetic group 41 cases had 72 arteriosclerotic relatives. In the non-diabetic group 38 patients had fifty-six arteriosclerotic relatives. Arteriosclerosis in the diabetic group preponderates on the paternal side, occurring almost twice as often as on the maternal side.

TABLE V.—41 CASES OUT OF 100 DIABETIC PATIENTS HAD 72 ARTERIOSCLEROTIC RELATIVES AS FOLLOWS:

| Paternal | | Maternal. | |
|---|---|---|---|
| Fathers | 16 | Mothers | 9 |
| Grandparents | 9 | Grandparents | 9 |
| Collateral | 17 | Collateral | 5 |
| Total | 42 | Total | 23 |
| Brothers and sisters | 7 | Children | 0 |

TABLE VI.—38 CASES OUT OF 100 NON-DIABETIC PATIENTS HAD 56 ARTERIOSCLEROTIC RELATIVES AS FOLLOWS:

| Paternal | | Maternal | |
|---|---|---|---|
| Fathers | 10 | Mothers | 7 |
| Grandparents | 7 | Grandparents | 11 |
| Collateral | 6 | Collateral | 10 |
| Total | 23 | Total | 28 |
| Brothers and sisters | 5 | Children | 0 |

In the family history of diabetics it is not uncommon to find arteriosclerosis in the paternal line and diabetes and obesity on the maternal side. These are strikingly illustrated by the following case summaries:

CASE 1644.—Female; aged thirty-six years. Diabetes. Diabetes in four maternal generations.

| Paternal. | Maternal. |
|---|---|
| Grandmother had arteriosclerosis | Grandmother had diabetes. |
| Father had arteriosclerosis | Mother had diabetes. |
| 2 aunts had arteriosclerosis. | Aunt had diabetes. |
| 2 uncles had arteriosclerosis. | |
| | 1 sister had diabetes. |
| | 1 brother had diabetes. |
| | 2 nephews had diabetes. |

CASE 1660.—Male; aged thirteen years. Diabetes. Diabetes in four maternal generations.

| Paternal. | Maternal. |
|---|---|
| Great-grandmother had cancer. | Great-grandmother had diabetes. |
| Father had arteriosclerosis. | Grandmother had diabetes and cancer. |
| | Mother had diabetes. |
| | Aunt had diabetes. |
| | Cousin had diabetes. |

CASE 1717.—Female; aged forty-eight years. Diabetes and arteriosclerosis.

| Paternal. | Maternal. |
|---|---|
| Father had arteriosclerosis. | Grandfather had arteriosclerosis (relatives all short lived). |
| 2 aunts had arteriosclerosis. | |
| | 1 brother had diabetes. |
| | 1 brother had cancer. |
| | 1 sister had arteriosclerosis. |
| | 1 nephew had diabetes. |
| | 1 daughter had neurosis. |

Similarly, obesity occurs more frequently in diabetic than in non-diabetic families, and maternal relatives are more often obese than are the paternal. Cancer occurs in one group about as often as in the other.

The most plausible explanation of the cause of diabetes is that advanced by Allen, namely, that the disease results from an exhaustion of the pancreatic cells. The facts here embodied are not

offered as proof that diabetes is inherited; they do justify the conclusion, however, that a favorable soil for the disease is created in the offspring of those afflicted either with diabetes or arteriosclerosis, or with both conbined, and to a lesser degree with obesity. Arteriosclerosis cannot be looked upon as a direct accountable factor because it is absent in diabetic children, although occurring frequently in their parents and grandparents. The very frequent association of diabetes and arteriosclerosis in middle-aged adults suggests a common cause and relationship, and that those agents which produce the one should be regarded as causal factors in the other. It is generally accepted that alcoholism, overeating, undue nerve strain, certain chemical, metabolic, and bacteriological intoxications, besides syphilis, may have etiological significance in the production of arterial degeneration. Of these deleterious agents infections must be seriously regarded. Arteriosclerotic individuals are very prone to infection, as are diabetics. So common are infections in these conditions that it is often quite difficult to say which is the more important or which antedates the other. Some workers in this field look upon diabetes as of bacterial origin. The frequency of occurrence of infection in the writer's series of cases is indicated in Table VII, in which are recorded only those infections which produce indubitable evidence of disease. Of these the most common are concealed infections in the teeth and tonsils.

TABLE VII.—A STUDY OF 100 DIABETIC PATIENTS, WITH REFERENCE TO ASSOCIATED SERIOUS INFECTION.

| Infection. | No. of cases. |
|---|---|
| Teeth and gums | 57 |
| Teeth and tonsils | 4 |
| Tonsils | 12 |
| Appendix | 6 |
| Gall-bladder | 4 |
| Ear | 1 |
| Other infections | 4 |
| Syphilis | 2 |
| Cases with no evident infection | 16 |
| Cases with onset after injury | 2 |

The true relation of infection to diabetes is not yet established. There are several possibilities, some of which are quite suggestive:

(*a*) It is possible that infection causes either the general arteriosclerosis which so commonly accompanies diabetes and thus leads to the premature involution of the individual; or

(*b*) A local sclerosis of the pancreas or other organs which have to do with food metabolism, according to Rosenow's elective affinity theory; or

(*c*) Acting as a fulminant it may precipitate a metabolic collapse by depressing the function of or otherwise incapacitating those organs of metabolism which may be inherently weak or have previously undergone sclerosis, also according to Rosenow's theory.

These opinions as to the relation of infection and sclerosis to diabetes, while largely conjectural, are in no small measure supported by clinical evidence and investigation. The following histories are submitted as cases in point:

CASE 1567.—Female; aged twenty years. Patient frail, delicate.

*Family History.* Father living at forty-five years; has diabetes. Mother died at thirty-eight years; cancer of uterus. One sister and one brother; both delicate. Maternal grandmother died at seventy-five years; arteriosclerosis and obesity. Weighed 268 pounds.

Patient for about three months had gastro-intestinal disease. When first seen on March 13, 1916, patient was suffering from an acute gastro-intestinal attack. Much pain and rigidity in right inguinal region. Nausea, vomiting, and constipation. Diagnosis of acute appendicitis made, which was confirmed by surgical counsel. History of intense thirst about two weeks previous. Former medical attendant claimed that urine before had always been sugar-free.

March 12, 1916. On general diet urine contained in fourteen-hour specimen 112 grams sugar, 2.6 grams ammonia. Patient presented evidence of impending coma.

March 14, 1916. Carbon dioxide tension of alveolar air 22.6 mm., Frederica apparatus. In a few weeks, symptoms of acute appendicitis subsided, acidosis disappeared, and food tolerance greatly increased. Then patient developed an acute tonsillitis and antrum infection which necessitated drainage operation. Coincident with this infection the food tolerance declined, acidosis developed, and the patient, while away from home, after an excessive indulgence in cake, candy, etc., died in coma. These data are graphically shown in accompanying chart.

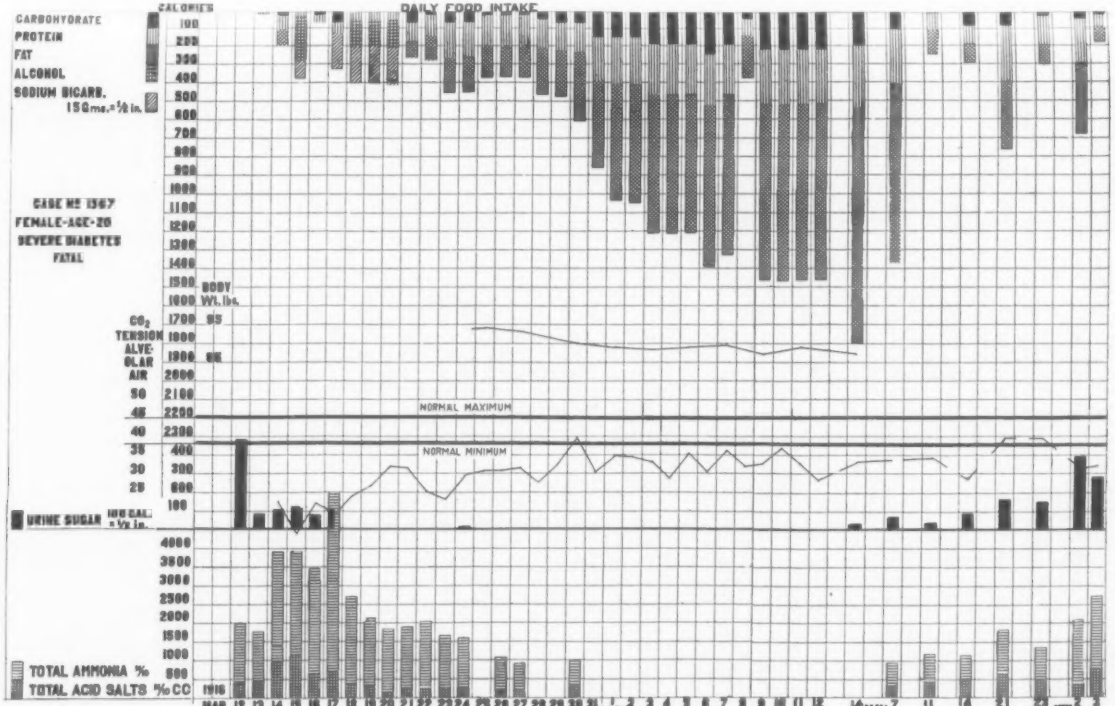
It would seem that this patient inherited the liability to diabetes. Whether or not the acute appendicular inflammation precipitated the metabolic collapse, while suggestive, is not capable of proof, there is no doubt, however, of the influence of that infection and the succeeding ones destroying the tolerance of the patient and precipitating coma and death.

Another case is equally suggestive:

CASE 1517.—Female; aged seventeen years. Patient pale, slender, poorly developed.

*Family History.* Incomplete and indefinite. Mother delicate, prematurely old, and a neurotic.

September, 1914. Patient had inserted in upper jaw an elaborate bridge-work which necessitated the crowning of several teeth. One month later she began to gradually fail. Thirst, polyuria, and loss of weight and strength followed. Urine not examined until after the lapse of one year, when patient was referred to writer. At that time her teeth gave evidence of well-marked dento-alveolar disease. Tonsils hypertrophied, degenerated, and


DAILY FOOD INTAKE
CALORIES
CARBOHYDRATE
PROTEIN
FAT
ALCOHOL
SODIUM BICARB. 15 Gms. = ½ in.
CASE NE 1367
FEMALE-AGE-26
SEVERE DIABETES
FATAL
BODY Wt. lbs.
$CO_2$ TENSION ALVEOLAR AIR
NORMAL MAXIMUM
NORMAL MINIMUM
URINE SUGAR 100 CAL. = ½ in.
TOTAL AMMONIA %
TOTAL ACID SALTS % CC
1916
MAR. 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31
APR. 1 2 3 4 5 6 7 8 9 10 11 12
14 MAY 7 11 14 21 28
JUNE 2 3

The data plotted hereon was designed to show the daily food intake and the effect of the diet as evidenced by the urine examination and lung air test. The food intake is plotted in calories, each food principle, including alcohol, having a different type of cross-hatching, as is indicated by the key. The total length of these several blocks represents the total caloric intake. Sodium bicarbonate is plotted in grams in which each subdivision, or one-half inch on the original chart, equals 15 grams. The carbon dioxide output of the lung air is plotted in millimeters of barometric tension. Urine sugar is plotted in calories on a base line so marked. Thus the carbohydrate intake can readily be compared with the carbohydrate loss or outgo. Urinary acid excretion is plotted in terms of decinormal alkali, as acid salts and ammonia, estimated by the Folin method. The sum of these is a fairly accurate expression of the total urinary acid excretion. From March 12 to March 24 the patient suffered severely from an acute attack of appendicitis. At the same time the patient exhibited a marked acidosis which gradually subsided as the gastro-intestinal disturbance disappeared. From April 1 to May 7 the diabetic condition improved materially; then the patient began to be tonsillar, and antrum infection set in which destroyed her food tolerance, so that from then on, even though on a low diet, she was in a state of negative balance. This chart strikingly illustrates the influence of infection on metabolism.

infected. Cervical lymph glands much enlarged, tongue swollen, and teeth marked. Patient in a state of advanced diabetes. Tonsils later enucleated, but parents objected to removal of insanitary bridge. Patient now has very little tolerance for food and remains in a state of low nutrition.

In this case the insertion of the bridge-work was immediately followed by dento-alveolar disease. Coincident with this came the diabetic symptoms. It is not unreasonable to assume that the impinging of this infection on a frail, poorly developed girl had something to do with the metabolic collapse which followed. These cases are not exceptional; they differ only in degree from many others which the writer might cite.

It is not the purpose of this paper to offer a new theory or to support or contest any of the older hypotheses as to the cause of diabetes but merely to emphasize to the clinician the importance of both arteriosclerosis and infection in diabetes. It would seem that the possible prevention or control of these factors would be a step in the direction of preventing the metabolic collapse which we call diabetes.

While the data herein submitted is insufficient and too limited to enable one to draw positive conclusions therefrom, it cannot be denied that it is extremely suggestive. In the mind of the writer it justifies the belief that:

1. The liability to arteriosclerosis and diabetes are transmissible from parent to offspring.

2. Infection, both acute and chronic, may precipitate a metabolic collapse or sufficiently lower the function of food metabolism in an individual with either general or local arteriosclerosis as to produce the clinical phenomena which we call diabetes.

3. Individuals with a family history of arteriosclerosis, diabetes, and obesity should be safeguarded against all latent and concealed or focal infections. Special attention should be directed to the head, so that dead teeth, apical abscesses, incompletely filled root canals, inflamed gums, infected and diseased tonsils, sinus and middle-ear disease should not exist.

4. Such individuals should be safeguarded in every way against those conditions which induce or hasten the arteriosclerotic process. Perhaps it is not going too far to say that individuals with an arteriosclerotic family history should not marry into diabetic families. Such a union is too frequently fraught with disaster to have it regarded with indifference. In the event of such marriage, until it can be proved otherwise, the children from this union should be carefully safeguarded along the lines indicated.

Medical literature affords little help as to how diabetes may be prevented. In view of the great and apparently increasing prevalence of the disease the writer has reported this limited investigation with the hope of stimulating further and more exhaustive inquiry in this direction.

# A STUDY OF THERMIC FEVER, WITH SPECIAL REFERENCE TO THE BLOOD AND URINE CHEMICAL FINDINGS.

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and

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Thermic fever is a term applied to certain symptom-complexes that are the result of disturbances of heat regulation, primarily from physical causes, the heat and water content of the air about the body, the condition of the peripheral vascular circulation, etc.; but these causes lead to chemical changes in the organism which are manifested in the characteristic clinical symptoms (auto-intoxication and retention) which, for a matter of classification, we would divide into two classes, namely, mild (due to overwork, bad ventilation, anxiety, worry, uncleanliness) and the severe (due to excesses, such as overeating and alcoholism). The causes of all are obviously the same. From a clinical stand-point we call those "mild" cases which reach a temperature of 107° or under and "severe" those which go above that point.

Taking the whole series of cases which may be included in the group, sunstroke and those due to heat prostration which occur in the absence of direct sunlight, we may state that insolation may occur under any circumstances in which heat accumulates in the body, and in which the body does not rid itself of its metabolic end-products such as urea, nitrogen, creatinin, and uric acid.

Hirsch[1] believed that while heat was the primary factor the immediate cause of the trouble was diminution of oxygen and retention of toxic principles. Vincent[2] also states his belief in a toxic basis. Gordon[3] says that recent work tends to the conception of paralyzing action on the nervous system of some toxic element which produces metabolic changes in the neurons, and according to the degree of auto-intoxication the effect of the sunstroke will be either an attack of ordinary heat-prostration or syncope, with unconsciousness or death.

If this be true, then insolation is an auto-intoxication brought about by substances formed in the body under abnormal conditions of heat retention as shown in our findings below. We wish in our figures on blood chemical changes to particularly emphasize the

[1] Quoted by Gordon: Osler, Modern Medicine, 1907, i, 52.
[2] Ibid.
[3] Osler: Modern Medicine, 1907, i, 52 (and R. G. Pearce, xxii, 525).

undue retention in these cases of the non-nitrogenous constituents of proteid metabolism.

The following cases occurred in the service of one of us (Schisler) in the St. Louis City Hospital.

## CLINICAL HISTORIES AND LABORATORY DATA.

Evans: male; aged fifty years; brewery worker; habits irregular; entered 5.30 P.M. August 5, 1916; unconscious; temperature, 110.4° (rectal); pulse, 130; respiration, 36; pupils contracted, reaction to light negative; general spasticity of body present; knee-jerks increased; toe signs questionable. The average blood-pressure taken during observation was systolic 91, diastolic 46 (Tycos); 30 c.c. spinal fluid (under normal pressure) was negative (Wassermann); urine albumin +++; many granular and pus casts. The man developed several generalized convulsions; pulse gradually became weaker; died August 6. No autopsy.

*Summary.* The question of uremia was thought of; this was ruled out because of the low blood-pressure. Cerebrospinal lues was questionable, the spinal fluid being negative. Diagnosis: thermic fever. No blood data on this case.

Muich: male; aged forty-five years; laborer; habits irregular; entered 4.45 P.M. July 30, 1916; unconscious; temperature, 108.6° (rectal); pulse, 110; irregular respiration, 48; pupils reacting to light; no rigidity or convulsions; heart irregular, with no positive findings; reflexes sluggish; stool and urine involuntary; emesis greenish-colored fluid; blood-pressure (systolic), 100; developed alcoholic psychosis and marked hallucinations; became rational four days after entering, when he gave a history of previous attack of thermic fever. Recovered, leaving hospital August 6, 1916.

August 4. Urine, no data.

Blood: Urea nitrogen, 19 mgm. per 100 c.c.; uric acid, 3.3 mgm. per 100 c.c.; creatinin, 3 mgm. per 100 c.c.; sugar, 0.138 per cent.

*Summary.* Observation made when convalescent; retention not great. It will be noted that this case while it displayed severe clinical symptoms did not show in its blood chemistry any cause for making a fatal prognosis. His urea nitrogen was 19, uric acid 3.3, creatinin 3 mgm., blood-sugar, 0.138 per cent.; values slightly above normal. It must be remembered that his urinary findings were the same as those of the cases that died and the other cases that recovered, namely, albumin and casts.

Ship: white; male; aged fifty-three years; bartender; habits irregular; entered 6.15 P.M. July 31, 1916; unconscious; temperature 108.2° (rectal); pulse, 180; irregular; respiration 40, labored; systolic murmur of apex; contraction of heart poor; pupils contracted, reaction to light sluggish but equal; regained consciousness on the second day but remained irrational. Developed alcoholic

psychosis; on the fourth day a secondary rise in temperature of 104.2° (axilla) and generalized convulsions; died August 4, 1916. No autopsy. Note the marked retention in the laboratory report below:

August 3. Urine: Albumin, very faint trace; sugar, negative; acetone, negative; diacetic acid, negative; indican, moderate amount.

Blood: Urea nitrogen, 76 mgm. per 100 c.c.; uric acid, 14.8 mgm. per 100 c.c.; creatinin, 6.1 mgm. per 100 c.c.; sugar, 0.177 per cent.

*Summary.* Moderate number of epithelial cells and leukocytes; very occasional red blood cells; two finely granular casts found after a prolonged search; clinical signs good; retention high, attracting attention to fatal prognosis. Died one day later.

It was noted in this case that his original symptomatology did not attract our attention to any fatal ending. On the contrary he seemed in rather good shape. He entered on July 31. On August 3 his blood findings showed high retention, the most significant observation in the same being the creatinin value of 6.1 mgm. This observation was made from blood obtained in the morning. On the following morning he died.

Huth: white; male; aged forty-two; concrete worker; habits irregular; entered 6.15 P.M. July 29, 1916; unconscious; temperature, 108.2°; pulse, 170, regular; respiration, 36; generalized convulsions; labored breathing; pupils contracted; reaction sluggish; knee-jerks increased; toe signs questionable; developed second rise in temperature and alcoholic psychosis; regained consciousness the fourth day. Average blood-pressure, 120. Discharged, well, August 26, 1916.

August 2. Urine: Albumin, moderate amount; sugar, negative; acetone, small amount; diacetic acid, small amount; indican, moderate amount.

Blood: Urea nitrogen, 26 mgm. per 100 c.c.; uric acid, 9.6 mgm. per 100 c.c.; creatinin, 3.83 mgm. per 100 c.c.; sugar, 0.168 per cent.

August 12. Urine: Albumin, negative; sugar, negative; acetone, negative; diacetic acid, negative; indican, negative.

Blood: Urea nitrogen, 14 mgm, per 100 c.c.; uric acid, 3.3 mgm. per 100 c.c.; creatinin, 2 mgm. per 100 c.c.; sugar, 0.12 per cent.

*Summary.* Moderate number of coarsely and finely granular casts and occasional leukocytes; very occasional leukocyte. Retention not high; patient recovered, although clinical signs seemed bad. This is an interesting case in that his symptoms were very severe, and yet blood chemical findings at this time did not indicate much retention, an observation which was well borne out by later tests and the ultimate fate of this case. On the tenth day of his stay in the hospital his blood findings were practically normal and his recovery certain. He was discharged on the twenty-eighth day of his stay.

O'Connor: white; male; brewery worker; habits irregular; married; entered 4.40 P.M. July 31, 1916; unconscious; temperature, 110.5°; pulse, 160, thready in character; respiration, 44, labored; heart action very weak; pupils markedly contracted, no reaction; generalized convulsions, with marked spasticity; did not regain consciousness; lumbar puncture made and 35 c.c. of clear fluid under normal pressure was obtained; became progressively worse; died 8.20 P.M. August 1, 1916.

August 1. Urine: Specific gravity, 1015; albumin, moderate amount; sugar, negative; acetone, negative; diacetic acid, negative; indican, very large amount. Serious findings.

Blood: Urea nitrogen, 33 mgm. per 100 c.c.; uric acid, 1.32 mgm. per 100 c.c.; creatinin, 4.8 mgm. per 100 c.c.; sugar, 1.5 per cent.

*Summary.* Moderate number of coarsely granular casts and red blood cells; occasional leukocytes. Retention high; patient died same day. We might call attention to our observations above on Ship case as applying in all particulars to this case.

Fischer: white; male; aged forty years; plumber; married; habits irregular; entered 8.50 P.M. July 30, 1916; unconscious; temperature, 109° (rectal); pulse, 150, regular but weak; respiration, 30; breathing irregular and labored; pupils dilated, reaction very sluggish; knee-jerks sluggish; toe signs questionable; general spasticity of body present; became conscious on third day but irrational; developed convulsions of a generalized type. The blood-pressure taken at intervals was systolic, 109, diastolic, 87 mm. The white blood count was 10,000; Wassermann blood and spinal fluid negative.

August 2. Urine: Albumin, very large amount; sugar, negative; acetone, moderate amount; diacetic acid, moderate amount; indican, moderate amount.

August 8. Urine: Albumin, negative; sugar, negative; acetone, negative; diacetic acid, negative; indican, trace.

August 12. Urine: Albumin, negative; sugar, negative; acetone, negative; diacetic acid, negative; indican, very large amount.

August 2. Blood: Urea nitrogen, 32 mgm. per 100 c.c.; uric acid, 8.6 mgm. per 100 c.c.; creatinin, 4.1 mgm. per 100 c.c.; sugar, 0.162 per cent.

August 3. Blood: Urea nitrogen, 39 mgm. per 100 c.c.; uric acid, 9.8 mgm. per 100 c.c.; creatinin, 4.56 mgm. per 100 c.c.; sugar, 0.165 per cent.

August 4. Blood: Urea nitrogen, 39 mgm. per 100 c.c.; uric acid, 7.9 mgm. per 100 c.c.; creatinin, 4.47 mgm. per 100 c.c.; sugar, 0.18 per cent.

August 8. Blood: Urea nitrogen, 45 mgm. per 100 c.c.; uric acid, 7.1 mgm. per 100 c.c.; creatinin, 3.94 mgm. per 100 c.c.; sugar, 0.156 per cent.

August 8. Spinal fluid: Urea nitrogen, 44 mgm. per 100 c.c.; uric

acid, 0.88 mgm. per 100 c.c.; creatinin, 2.4 mgm. per 100 c.c.; sugar, 0.1 per cent.

August 10. Blood: Urea nitrogen, 55 mgm. per 100 c.c.; uric acid, 6.9 mgm. per 100 c.c.; creatinin, 5 mgm. per 100 c.c.; sugar, 0.174 per cent.

August 12. Blood: Urea nitrogen, 89 mgm. per 100 c.c.; uric acid, 8.2 mgm. per 100 c.c.; creatinin, 5 mgm. per 100 c.c.; sugar, 0.2 per cent.

*Summary.* Urinary findings indicated some marked renal disturbance, but not of the same importance as blood findings. Remarkable number of casts on last day of life. High retention, indicating probable fatal outcome. Patient died two days after creatinin reached 5 mgm. per 100 c.c. This was the most interesting case of our series, because it showed the typical high retention, gradually increasing, of all the constituents, finally reaching the fatal "creatinin" point of 5 mgm. Again, this patient lived fourteen days in practically an unconscious state, finally dying with the findings at autopsy above catalogued. It is also to be noted that the macroscopic and microscopic findings, particularly of the kidneys, showed nothing chronic, simply a cloudy swelling and possible passive congestion. This, of course, rules out the possibility of the blood retention in this case, being due to any pre-existing renal deficiency.

Postmortem examination of this case was made by Dr. D. F. Hochdoerfer, whose courtesy in demonstrating the gross changes we wish to acknowledge.

The complete autopsy report follows:

Color, white; sex, male; height, 5 feet 8 inches; weight, 130 pounds; hair, blond; eyes, gray.

External appearance: No evidence of external violence. Body emaciated.

Rigor mortis: Present.

Scalp: Normal.

Skull: Normal.

Membranes of brain: Thickened and adherent.

Brain: Watery and anemic.

Spine and spinal cord: Spine normal. Spinal cord at cervical section normal.

Pleural cavities: Adhesions right cavity.

Lungs: Pneumonic areas in right lower lobe. Bronchi filled with bloody, watery secretion. Right lung on section contained a large amount of watery exudate. All evidence of a bronchopneumonia present.

Intestines: Normal.

Liver: Fatty.

Spleen: Small.

Pancreas: Normal.

Kidneys: Parenchymatous and interstitial changes present. Cloudy swelling. Capsule slightly adherent.

Bladder: Normal.

Male genitalia: Normal.

Remarks: History, insolation July 30, with temperature 107°.

Pieces of the various organs were taken for microscopic examination, namely, brain, heart, spleen, pancreas, liver, and kidneys. The most definite changes were seen in the kidney structure. Here we had a typical picture of cloudy swelling without any of the well-marked changes of a preëxisting or long-standing degeneration.

The gross and microscopic changes in this case indicate a simple passive congestion of the kidneys and the usual absence of gross or minute manifestations as commonly seen in thermic fever.

We give below a summary of the blood and urinary findings in these cases.

**BLOOD ANALYSIS** / **URINE ANALYSIS***

| CASE | DATE | OUTCOME | UREA NITROGEN mgms. per 100 cc. | URIC ACID mgms. per 100 cc. | CREATININE mgms. per 100 cc. | SUGAR mgms. per 100 cc. | REMARKS | SPECIFIC GRAVITY | ALBUMIN | SUGAR | ACETONE | DIACETIC ACID | INDICAN | MICROSCOPICAL EXAMINATION | REMARKS |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| O'Conner | 8/1 | DIED | 33 | 13.2 | 4.8 | 150 | RETENTION HIGH. PATIENT DIED SAME DAY. | 1015 | # | Neg. | Neg. | Neg. | ### | Moderate number of coarsely granular casts and red blood cells. Occasional leucocytes. | FINDINGS SERIOUS |
| Fischer | 8/2 | | 32 | 8.6 | 4.1 | 0.167 | High retention indicating probable fatal outcome. Patient died two days after creatinine reached 5.0 mgms. per 100 cc. | | ### | Neg. | # | # | # | Moderate number of granular casts and epithelial cells. | Urinary findings indicated some marked renal disturbance, but not same importance as blood findings. |
| | 8/3 | DIED | 39 | 9.8 | 4.56 | 0.165 | | | | | | | | | |
| | 8/4 | | 39 | 7.9 | 4.47 | 0.180 | | | | | | | | | |
| | 8/8 | | 45 | 7.1 | 3.99 | 0.154 | | | Very | Neg. | Neg. | Neg. | Trace | Moderate number of epithelial cells leucocytes and finely granular casts. | |
| | 8/11 | | 44 | 0.88 | 2.4 | 0.10 | | | | | | | | | |
| | 8/10 | | 55 | 6.9 | 5.0 | 0.174 | | | | | | | | | |
| | 8/12 | | 89 | 8.2 | 5.0 | 0.220 | | | Very | Neg. | Neg. | Neg. | ### | Very many granular casts and occasional leucocytes. Such number of casts is rarely seen | Remarkable number of casts on last day of life. |
| Huth | 8/2 | RECOVERED | 26 | 9.6 | 3.85 | 0.160 | Retention not high. Patient recovered although clinical signs seemed bad. | | # | Neg. | + | + | # | Moderate number of coarsely and finely granular casts and occasional leucocytes. | |
| | 8/12 | | 14 | 3.3 | 2.0 | 0.120 | | | Neg. | Neg. | Neg. | Neg. | Neg. | Very occasional leucocyte. | |
| Ship | 8/3 | DIED | 76 | 14.8 | 6.1 | 0.167 | Clinical signs good. Retention high, attracting attention to fatal prognosis. Died one day later. | Very low | Neg. | Neg. | Neg. | Neg. | # | Moderate number of epithelial cells and leucocytes. Very occasional red blood cells. Few finely granular casts found after a prolonged search. | |
| Huich | 8/14 | RECOVERED | 19 | 3.3 | 3.0 | 0.110 | Observation made when convalescent. | | | | | | | | |

* ### Very large amount
\# Moderate amount
+ Small amount.

FIG. 1

For purposes of comparison we give a charted description of the blood changes in some of the well-known conditions in which the microchemical methods of Folin, Denis, Benedict, Lewis, Myers, and Fine have been worked out.

In passing it might be added that the blood-chemical analyses were made following the technic that has been elaborated by Folin and others. The blood was uniformly taken in the morning before nourishment was given. It was procured from one of the superficial veins on the forearm, received into potassium oxalate and defibrinated. A portion was precipitated at once with picric acid

for sugar and creatinin estimations, the balance being used for the urea-nitrogen and uric-acid determinations. For the sugar estimations we used the method of Benedict and Lewis;[4] for the creatinin, the method of Folin;[5] for the urea, the urease method of Marshall[6] and Van Slyke;[7] for the uric acid, the method of Folin[8] modified by Benedict.[9] In all cases we used the Hellige instrument in making our determinations.

THE CHARACTERISTIC BLOOD PICTURES IN GOUT, DIABETES & NEPHRITIS II { UREA N, URIC ACID, CREATININE & SUGAR }

| DISEASE | UREA N. | URIC ACID | CREATININE | SUGAR |
|---|---|---|---|---|
| | MGMS. PER 100cc of BLOOD | | | PER CENT |
| NORMAL | 12-15 | 1-3 | 1-2.5 | 0.08-0.12 |
| GOUT | | 3.5-6 | | |
| MILD DIABETES | | | | 0.15-0.30 |
| SEVERE DIABETES | | | | 0.30-1.10 |
| CHRONIC NEPHRITIS | 15-50 | 1-4 | 1-3 | |
| UREMIC NEPHRITIS | 80-300 | 4-15 | 4-34 | 0.10-0.20 |
| THERMIC FEVER | UREA N 26-89 | URIC ACID 6-14 | CREATININE 3-6.1 | SUGAR 0.15-0.20 |

FIG. 2

CONCLUSIONS. The study of these cases from the laboratory stand-point has been most instructive. Here we have in thermic fever a condition that is unquestionably analogous in its symptomatology to some form of uremia. Again, we have in the urinary findings a close resemblance to this condition. We found in the blood-chemical analyses of these cases high retention of the non-protein nitrogen constituents, indicating clearly a deficiency of renal function. In some cases the retention was high and the symptomatology not bad, yet these cases died. In other cases we found low retention and bad symptoms, and the patients uniformly recovered. Is this not then a truer guide to the exact status of the patient from the stand-point of prognosis than the data obtainable either from the clinic or urinary analysis? We do not wish by any means to insinuate that the whole course of any

[4] Jour. Biol. Chem., 1915, xx, 61.
[5] Jour. Biol. Chem., 1913, xv, 487.
[6] Proc. Ann. Soc. Biol. Chem., 1915.
[7] Am. Jour. Physiol., 1905, xiii, 45.
[8] Ibid., 1914, xix, 211.
[9] Jour. Biol. Chem., 1915, xx, 629.

case can be completely predicated upon the blood-chemical findings, but we do insist upon the great value of this work in this and allied conditions. The determination of the amount of creatinin in these cases has given us some figures which seem to bear out the contention of Myers and Lough[10] that a percentage of creatinin that exceeds 5 mgm. per 100 c.c. of blood bodes ill for the patient. It will be noted that in the cases of O'Connor, Fischer, and Ship we had a creatinin value around or above 5 mgm. These three cases died. In the case of Ship at the time his blood was taken his clinical condition did not seem to be nearly as bad as that of Huth, yet the creatinin value of the former was above the so-called fatal point, whereas the latter had only a creatinin retention of 3.83 mgm. The of case Ship, however, vindicated the prognostic value of a high creatinin retention, as he died on the morning following this determination, yet Huth, whose blood-creatinin was 3.83 at the time that his clinical condition seemed to point to a fatal ending, recovered, showing ten days later practically normal blood figures. Thermic fever can be added therefore to the set of conditions which with high creatinin value, 5 mgm. or over, can be said to offer a fatal prognosis. For all intents and purposes these figures in thermic fever may be construed as similar in their interpretation to those obtained in severe uremic nephritis.

TREATMENT. A word or two in regard to the treatment of these cases: tub baths, gradually cooling the water to ice bath until the patient's temperature was reduced to 104° or under; stimulation with camphor, strychnin, and digitalin, free elimination, proctoclysis, with normal saline solution. In general, symptomatic treatment.

We wish to extend our thanks to Mr. A. J. Blaivas for valuable assistance in the chemical analyses and to Drs. Irvin Schmidt and W. I. Smith, of the staff of the hospital, for their active coöperation.

## THE CLASSIFICATION OF THE CHRONIC HIGH BLOOD-PRESSURE CASES.

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THERE is no subject in medicine which, in the present age, has more vital interest to physicians than that of the chronic diseases of the circulatory system. Figures in all vital statistics have shown us that all affections of the circulatory and renal systems are definitely on the increase. "Arterial diseases of various kinds,

[10] Arch. Int. Med., 1915, xvi, 536–546.

atheroma, aneurysm, etc., caused 15,685 deaths in 1915, or 23.3 per 100,000. This rate, although somewhat lower than the corresponding ones for 1912 and 1913, is higher than that for 1914, and is very much higher than that for 1900, which was 6.1."[1] True, the average length of life has been considerably prolonged in the past twenty-five years, yet it is not due to a decrease in the incidence of these chronic diseases. We are not absolutely certain yet of the causes which are concerned in the increase of the chronic affections of the circulatory and renal systems, but our modern life, with its stress and strain, its mental concentration and overindulgence in protein food, must have some large part in the production of these diseases.

The study of the cardiovascular system has been greatly advanced by the introduction of instruments of precision which measure the blood-pressure, record the radial pulse, the venous pulse, the venous pressure, and record on photographic paper or film the electrical variations of the parts of the heart. Again, the introduction of various tests to measure the functional capacity of the kidneys has added immensely to our knowledge of various kidney diseases, and has been of great help in prognosis. To keep pace with the advances in these closely allied branches of medicine taxes the time and energy of any man. All that we can hope to do is to gather together a few of the generalizations and apply them as best we can to our daily work.

Blood-pressure as an aid to diagnosis has been badly used and much abused. Some have even expected the instrument to name the diagnosis, and when it, unlike Balaam's ass, was silent the instrument was blamed and discarded as worthless. Such an attitude is puerile. It is largely the result of taking only systolic pressure and neglecting the important diastolic and pulse-pressure. Happily this conception of blood-pressure is now undergoing a change, and we confidently expect to find that much help in diagnosis and prognosis will be given by careful blood-pressure estimations.

Five so-called phases have been described in the auscultatory blood-pressure phenomenon.[2] The systolic pressure is read at the beginning of the first phase and the diastolic, as I have shown,[3] is read at the sudden transition from the third to the fourth phase, or where the loud third sound suddenly becomes dulled. From there to the fifth phase, that is, no sound, is usually only from 4 to 6 mm. For those who find difficulty in determining the sudden transition of sound the fifth phase may be used. Hooker and Southworth[4] conclude from their observations that for clinical purposes the diastolic pressure may be taken at the disappearance of

[1] United States Mortality Statistics for 1915.
[2] Korotkov: Mitt. d. k. mil. med. Akad. zu St. Petersburg, 1905, xi, 365.
[3] Warfield, L. M.: Arch. Int. Med., 1912, x, 258.
[4] Arch. Int. Med., 1914, xiii, 384.

all sounds (the fifth phase). I have called attention, however, to the fact that in cases of aortic insufficiency there is no fifth phase, that is, the fourth phase or dull tone is heard over the uncompressed artery, hence one could not use the point of disappearance of sound to determine diastolic pressure. Must one then conclude that there is no diastolic pressure in aortic insufficiency? That would be absurd. One can easily obtain the diastolic pressure by taking the sudden transition of third into fourth phase. As a matter of fact, except in cases of aortic insufficiency, one may use the fifth phase to determine the diastolic pressure. It must, however, be remembered that there is an error of 4 to 6 mm. normally and up to 16 mm. in high-pressure cases.[5]

In an irregular heart, especially in the cases due to myocardial disease, it is quite impossible to determine the true diastolic pressure. One can only approximate it and say that the pulse-pressure is low or high. As a matter of fact the real systolic pressure cannot be determined. For this figure the place on the scale where most of the beats are heard may be taken for the average systolic pressure. No one can seriously maintain that he can measure the diastolic pressure under all circumstances.

By means of the auscultatory method of measuring blood-pressure we are able to determine irregularities of force in the heart beats more easily than by listening to the heart sounds. A pulsus alternans is readily made out. The irregular tones heard over the brachial artery in cases of irregular heart action have been called "tonal arrhythmias."[6]

There are three parts to every blood-pressure estimation: the systolic, the diastolic, and the pulse-pressure. These I have called the pressure picture.[7] To these should be added the pulse-rate in order to make the reading complete. Obviously, to say that the systolic pressure is 140, 160, or 200 mm. Hg. conveys to more knowledge of what the heart is doing than a count of red cells alone determines the kind of anemia. We have long known that a great variety of influences modifies the systolic pressure. Some of the influences are psychic and are entirely beyond our or the patient's control. Some apparently trivial circumstances, a chance remark made to the patient, an occurrence earlier in the day the memory of which flashed through his mind, may and does increase the systolic pressure 20 mm. or more above the average normal for the person. The systolic pressure measures the total work of the heart at the moment when it is tested. In a few minutes it may be higher or lower. A pathological or, rather, a compensatory high systolic pressure is always high, but the height is subject to great variation which makes it unwise to attribute a drop in pressure to any therapeutic measure.

[5] Warfield, L. M.: Jour. Am. Med. Assn., 1913, lxi, 1254.
[6] Goodman and Howell: Am. Jour. Med. Sc., 1911, cxlii, 324.
[7] Warfield, L. M.: Ibid., 1914, cxlviii, 880.

The diastolic pressure measures the peripheral resistance. It measures the work of the heart, the potential energy,[8] up to the moment of the opening of the aortic valves. It is the actual pressure in the aorta. The diastolic pressure is not very variable; it is not subject to the same influences which disturb the systolic pressure. It fluctuates, as a rule, within a small range. It is not affected by diet, by mental excitement, by subconscious psychic influences, to anything like the extent to which the systolic pressure is affected by the action of these factors. The diastolic pressure is determined by the tone in the arterioles and is under the control of the vasomotor sympathetic system. Any agent which causes chronic irritation of the whole vasomotor system produces increase in the peripheral resistance with consequent rise in the diastolic pressure. Any agent which acts to produce thickening of the walls of the arterioles, narrowing their lumina, produces the same effect.

Such states naturally result in increased work on the part of the heart, which, as a result, hypertrophies in the left ventricle. The increase in size and strength is a compensatory process in order to keep the tissues supplied with their requisite quota of blood. Conversely, paralysis of the vasomotor system produces fall of diastolic pressure which, if long continued, results in death.

The diastolic pressure then is of importance for the following reasons:

1. It measures peripheral resistance.
2. It is the measure of the tonus of the vasomotor system.
3. It is one of the points to determine pulse-pressure.
4. Pulse-pressure measures the actual driving force, the kinetic energy of the heart.
5. It enables us to judge of the volume output, for pulse-pressure (PP) $\times$ pulse-rate (PR) = volume output in most instances.
6. It is more stable than the systolic pressure, subject to fewer more or less unknown influences.
7. It is increased by exercise.
8. It is increased by conditions which increase peripheral resistance.
9. The gradual increase of diastolic pressure means harder work for the heart to supply the parts of the body with blood.
10. Increased diastolic pressure is always accompanied by increased pulse-pressure and increased size of the left ventricle, temporarily (exercise) or permanently.
11. Decreased diastolic pressure goes hand in hand with vasomotor relaxation, as in fevers, etc.
12. Low diastolic pressure is frequently pathognomonic of aortic insufficiency.
13. When the systolic and diastolic pressures approach, heart failure is imminent either when pressure picture is high or low.

[8] Stone, W. J.: Arch. Int. Med., 1915, xvi, 775.

Pulse-pressure measures the actual head of pressure which maintains the circulation, the force driving the blood to the periphery. As the circulatory bed widens the pulse-pressure diminishes until at the capillaries it is only about 5 mm. Hg.

When all these factors are taken into consideration it becomes apparent that the diastolic pressure is most important, if not the most important, part of the pressure picture. I am not unaware of the value of the great mass of statistical evidence which shows the bad prognostic import of high systolic pressure alone. One could show by the red cell count alone the seriousness of the low count, but one would fail to differentiate types of anemia and be unable to offer really valuable evidences of the gravity of anemia. So while conclusions drawn from statistics of high systolic pressure are in general correct, there is necessarily much that is incorrect and grossly misleading in them. I feel that only when we study our cases with the whole pressure pictures before us will we be able to draw really valuable conclusions for everyday use.

Figures for the normal pressure picture vary somewhat with sex and age. In adults we may safely assume that a systolic pressure which is constantly over 150 mm. Hg. is abnormal; a diastolic constantly over 90 is abnormal and a pulse-pressure over 50 mm. is an increased pressure.

Normally the pulse-pressure varies from 30 or under, low to 50 or above, high. We have found that in all of the cases of high pulse-pressure the left ventricle was dilated—it actually held more blood than a normal ventricle holds. The arch of the aorta was also dilated, easily revealed by auscultating over the manubrium,[9] and the seat of a definite sclerosis which rendered it less capable of expansion when the blood from the left ventricle was thrown into it at systole. The sequence of events conjecturally is as follows: There is arteriosclerosis of the aorta (usually the nodular), diffuse thickening of the walls of the large arteries, also some concomitant fibrous change in the myocardium. The elasticity of the aorta is reduced, hence the evenly distributed force which normally keeps the blood moving between systoles is absent. In order for the circulation to be carried on out to the extreme periphery, so that all the organs receive blood, more blood must be thrown at each systole into the aorta. The force also must be greater because the distributing tubes are no longer capable of doing their full share in maintaining the circulation in equilibrium. This not only causes hypertrophy of the left ventricle but actual increase of size of the cavity of the ventricle in order to accommodate the added amount of blood which must be put out at systole. As a result the left ventricle hypertrophies and dilates. The pathological process which is present in the myocardium by its very nature tends to increase gradually. More muscle fibers

[9] Warfield, L. M.: Jour. Am. Med. Assn., 1917, lxviii, 824.

are destroyed, more dilatation supervenes, more compensatory hypertrophy of the remaining fibers takes place. A vicious circle thus becomes established until finally the heart loses the power of carrying on the circulation and decompensation sets in. While we cannot prove this sequence absolutely, we believe that our clinical studies and our pathological studies make it more than probable that events occur in the order in which they have been related.

Again, the diastolic pressure, the peripheral resistance, does not rise in these cases above 110 mm. Usually it is between 90 and 100 mm. The systolic rarely goes above 200 mm. The pulse-pressure then may be from 80 to 110 mm. The larger the pulse-pressure the greater the cavity of the left ventricle and the more dilated is the arch of the aorta.

Stone[10] has divided the cases of hypertension into the cerebral and cardiac types. He finds there is a difference in prognosis and in mode of death in the two groups. He thinks that the pressure-ratio (heart load) which he has made use of will enable one to determine the type of case. I cannot say that I have found his method applicable except to a very few cases, although I agree with him in his contention that such a separation of cases is possible. I have felt the need of a better classification of the cases of chronic hypertension. For the past few years the cases have been critically studied, and it is believed that Stone's first group is composed of two groups, in general usually differentiable. I should therefore propose a classification into three groups. Syphilis is not an etiological factor in these cases. It is not contended that these groups are absolutely distinct. There are variations and combinations which render an exact separation into groups impossible. Bearing this in mind the following classification of the chronic high blood-pressure cases is submitted.

Group A. *Chronic Nephritis.* These are the cases with a high-pressure picture, that is to say, high systolic (200+) and high diastolic (120–140+). The pulse-pressure is much increased. The palpable arteries are hard and fibrous. There is puffiness of the under eyelids, which is more pronounced in the morning on arising. Polyuria with low specific gravity and nycturia are present. There are almost constant traces of albumin in the urine, with hyaline and finely granular casts.

Functionally these kidneys are much under normal. The functional capacity determined by Mosenthal's modification of the Schlayer-Hedinger method shows a marked inability to concentrate salts and nitrogen. The phthalein output is below normal. As the case advances the phthalein output becomes less and less until a period is reached when there are only traces or complete suppression

[10] Loc. cit.

at the end of a two-hour period. Such patients may live for ten weeks (one of our cases), all the time showing mild uremic symptoms, and suddenly pass into coma and die.

The natural end of patients in this group is either uremia or cardiac decompensation (so-called cardiorenal disease). Cerebral accidents may happen to a small number. It is only to this group, in my opinion, that the term cardiorenal disease should be applied. Formerly I believed that all high systolic pressure cases were cases of chronic nephritis of some definite degree. From the purely pathological stand-point that is true, but from the real, the functional stand-point, it is far from being the true state of the cases.

In this group there is marked hypertrophy and moderate dilatation of the left ventricle with dilatation and nodular sclerosis of the aorta. The kidneys are firm, red, small, coarsely granular, the cortex much reduced, the capsule adherent. Cysts are common. It is the familiar primary contracted kidney. Mallory calls this capsular-glomerulo-nephritis. The etiology is obscure. Often no cause can be found. Again, there is a history of some kidney involvement following one of the acute infectious diseases, or it may follow the nephritis of pregnancy. Usually, however, these cases fall into the group of secondary contracted kidneys, chronic parenchymatous nephritis.

Case I.—R. Z., a woman, aged thirty-six years, was seen July 26, 1916, in coma. There was a history of typhoid fever at nineteen years, but no other disease. She had had nine full-term pregnancies, the last one thirteen months previously. For a week before the onset of the present illness she had complained of severe headaches and dizziness. There were no heart symptoms. For the past year she has had nycturia. Physical examination revealed tubular breathing beneath the manubrium, a few rales in the chest, an enlarged heart (left side), with a systolic murmur over the aortic area. Blood-pressure was 178–125–53, the pulse-rate 96, leukocytes 27,250. Venesection of 500 c.c. of blood and intravenous injections of 500 c.c. of 5 per cent. $NaHCO_3$ in normal saline were employed. Lumbar puncture withdrew 60 c.c. of clear fluid under pressure with 6 cells per cubic millimeter. The eye-grounds showed distinct haziness of the disks and dilatation of the veins. Blood-pressure after venesection was 164–122–42, pulse 76, but in a few days rose to 222–142–80, pulse 70. A second venesection of 400 c.c. and proctoclysis of 1000 c.c. saline solution was tried. The blood-pressure now was 198–140–58. The pH of the blood was 7.6, the alkaline reserve was 35 volume per cent. (van Slyke), and the $CO_2$ tension of the alveolar air (Marriott) was 25 mm. The phthalein on the day following the second venesection was 45 per cent. in two hours. The urine at first showed 500 c.c. in twenty-four hours, specific gravity 1016, albumin and casts. Later she passed 1300 to 1600 c.c., with specific gravity around 1010. The

blood-pressure fluctuated considerably, reaching as low as 138–98–40, pulse 88. She was discharged improved September 10, 1916. At present (March, 1917) she is doing all her housework, but occasionally has headaches and attacks of dizziness.

GROUP B. This one might designate as the hereditary type, although there is not always a history in the antecedent. This group includes the robust, florid, exuberantly healthy people. They often are heard to boast that they have never had a doctor in their lives. They are usually thick-set or very large, fleshy people. The pressure picture is exceedingly high. The pulse-pressure is moderately increased. The arteries are rather large, fibrous, and often quite tortuous, although this is not always the case. Some persons have hard, small fibrous arteries. There is no puffiness beneath the eyes, no polyuria, and no nycturia as a rule. The urine is of normal amount, color, and specific gravity. Albumin is only rarely found and then in traces, but careful search of a centrifuged specimen invariably reveals a few hyaline casts. The phthalein excretion is normal or only slightly reduced. The kidneys excrete salt and nitrogen normally. It is in this group that apoplexy is found most frequently. The rupture of the vessel occurs when the victim is in perfect health, often without any warning. Occasionally when such a case recovers sufficiently to be around, cardiac decompensation sets in later and he dies then of the cardiac complications.

Pathologically the hearts of such persons are found to have the most enormous hypertrophy of the wall of the left ventricle. The cavity is somewhat enlarged, as is always the case when the pulse-pressure is increased, but the size of the cavity is not the striking feature. The aorta is fibrous, thick walled, and the arch is slightly dilated. There are patches of arteriosclerosis. One such case seen only at autopsy had a rupture of the aorta just above the sinus of Valsalva and died of hemopericardium. The kidneys are of normal size, dark red, firm, the capsule strips readily, the surface is smooth or finely granular, the cortex is not decreased. The pyramids are congested and red streaks extend into the cortex. Microscopically the capsules of the glomeruli are a trifle thickened; a few show hyaline changes. There is rather diffuse, mild, round-cell infiltration between the tubules. The tubular epithelium shows little or no demonstrable changes. The arterioles are generally the seat of a moderate thickening of the intima and media, but it is not usual to find obliterating endarteritis. There is evidently a diffuse fibrous change which has not affected either the tubules or glomeruli to any great extent.

CASE II.—L. C., a man, aged fifty-six years, stonemason by trade, is a stocky, thick neck individual. He has never been ill in his life until a year ago, when he fell from his chair unconscious. He had a right-sided hemiplegia which has cleared up so completely that except for a very slight drag to his foot he walks

perfectly well. He came in complaining of shortness of breath and cough. There was no swelling of the feet. Here evidently was left-heart decompensation. Examination showed the blood-pressure to be 240–130, pulse irregular, 104 to the minute. There was cyanosis and rales throughout both chests. The urine was normal in color, specific gravity 1025, small amount of albumin, few casts, hyaline and granular. The phthalein elimination was 65 per cent. in two hours. Under rest, purgatives, and digitalis he was much improved. He has since had two other apoplectic strokes, the last of which was fatal.

When these patients are seen with acute cardiac decompensation there is, of course, much albumin and many casts in the urine, and the phthalein output is, for the time being, decreased.

Group C. This might be called the arteriosclerotic high-tension group. The cases are usually over fifty years old. They are men and women who have lived high and thought hard. Often they have had periods of great mental strain. Many men in this group were athletes in their young manhood. Many have been fairly heavy drinkers, although never drinking to excess. They are usually well nourished and inclined to stoutness. The pressure picture is high systolic with normal or only slightly increased diastolic and large pulse-pressure. The arteries are large, full, fibrous, usually tortuous. The heart is very large, the apex far down and out. There is no polyuria; nycturia is uncommon, quite the exception. The urine is normal in color, amount, and specific gravity. Albumin is only rarely found and hyaline casts are not invariably present. The phthalein excretion is quite normal and the excretion of salt and nitrogen are also normal. The terminal condition in most of the patients in this group is cardiac decompensation. They may have several attacks from which they recover, but after every attack the succeeding one is produced by less exertion than the preceding one, and it becomes more and more difficult to control attacks. Eventually the patients become bed- or chair-ridden, and finally die of acute dilatation of the heart.

Occasionally patients in this group may have a cerebral attack, but in my experience this is uncommon. Pathologically the heart is large, at times true cor bovinum, dilated and hypertrophied. The cavity of the left ventricle is much dilated. The aorta is dilated and sclerosed.

The kidneys are increased in size, are firm, dark red in color, with fatty streaks in the cortex. The capsule strips readily and the cortex is normal in thickness or only slightly increased. The organ offers some resistance to the knife. The microscope shows small areas scattered throughout where the glomeruli are hyalinized, the stroma full of small round cells, the tubules dilated, and the cells are almost bare of protoplasm. Naturally the tubules are full of granular cast material. Also the arterioles show extensive intimal

thickening, fibrous in character, with occasional obliterating endarteritis. One gets the impression that the small sclerotic lesions are the result of anemia and gradual replacement of scattered glomeruli by fibrous tissue. For the most part the kidney, except for the chronic passive congestion, appears quite normal. One can readily understand that in such a kidney function could not have been interfered with.

CASE III.—C. K., an active, stout, business man, aged fifty-six years, consulted me on account of shortness of breath and swelling of the feet in May, 1915. He had just returned from a hospital in another city, where he had gone with what was apparently cardiac decompensation. In his early manhood he had been a gymnast and was a prize winner. He has worked hard, often given way to violent paroxysms of temper, has eaten heavily but drunk very moderately. The heart was greatly enlarged, the arch of the aorta dilated, a mitral murmur was audible at the apex. The radials and temporals were large, tortuous, and fibrous. The blood-pressure picture ranged around 180–90–90. He was easily made dyspneic and had a tendency to swelling of the lower legs. The urine was acid, of normal specific gravity, normal in amount, normal phthalein, normal concentration of salt and nitrogen, contained albumin only when he was suffering from decompensation of the heart. Casts were always found. He finally died, after sixteen months, with all the symptoms of chronic myocardial insufficiency. The heart was enormous, a true cor bovinum. The kidneys were typical of this condition, possibly somewhat larger than usual.

The management of these groups of patients presents many difficulties. I believe that all these excessive pressures are compensatory. As has been said before, the systolic pressure is subject to considerable variations, but the diastolic remains fairly constant. Unless one can reduce the whole pressure picture therapy is useless. This reduction is far from being easy to accomplish. Occasionally one sees cases, such as two we have seen, in which there was uremia, high-pressure picture, almost total phthalein suppression. Eventually there was complete recovery, with normal pressure pictures. Such cases are the exceptions and are probably acutely toxic in origin. The chronic, slowly progressive cases do not act thus. The best we can do is to make searching inquiries into the mode of life and regulate it on a rational basis. All people of the three groups need regulation of habits and diet. We have not found drugs of value, with the possible exception of bichloride of mercury and potassium iodide. Even in the positive absence of syphilis these drugs in combination seem to exert a favorable influence on the factors which are causing the high pressure. Electricity in the form of the static current, the high-frequency current, and other forms are recommended. All aid in maintaining nutrition and hygiene, but in my experience have no permanent effect upon this class of cases which other measures do not have.

Naturally when decompensation sets in it is to be treated as it usually is in spite of the high systolic and high diastolic pressure. As a matter of fact I have seen the pressure picture reduced when compensation was restored under digitalis, and it is generally recognized that such is the case. Personally I believe that hydrotherapy, attention to the bowels, regular hours, great decrease in food, limitation of meats, especially purin base-containing meat products, substitution of buttermilk and cheese in the diet, are the chief means at our disposal for regulating the lives of those who fall into our hands before accidents have happened. But I realize that we have no means of actually preventing a cerebral hemorrhage, although we have some control over the development of a cardiac breakdown.

Finally, this grouping is of interest in respect to prognosis. Careful examination of the patient should enable us to predict with some degree of accuracy what will happen to him. We may be able to modify somewhat the course, and, in general, we can render a fairly correct prognosis. This is certainly of value to the patient's family as well as to the patient.

Conclusions. 1. In a blood-pressure reading the whole record should be taken, systolic, diastolic, pulse-pressure, and pulse-rate. The pressure picture is the term suggested for the figures representing the component parts of the blood-pressure reading.

2. The diastolic and pulse-pressure give us more information than the systolic pressure.

3. There are three groups of high-pressure cases, called (A) chronic interstitial nephritis, (B) hereditary or cerebral type, (C) arteriosclerotic or cardiac type. Causes of death are usually anemia in group A, cerebral hemorrhage in group B, and cardiac decompensation in group C.

4. The term cardiorenal disease should be reserved for the cases of group A, which suffer from cardiac decompensation; the term hypertensive cardiovascular disease for cases of group B. Myocardial insufficiency covers most of the cases in group C.

5. Prognosis is much more intelligently given when this grouping of cases is followed.

# A STUDY OF CASES OF ASCITES IN THE WARDS OF THE CANTON HOSPITAL, CHINA.

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A visitor to the medical wards of the Canton Hospital is always impressed with the large number of patients suffering from ascites. While the majority of patients admitted to the hospital are surgical, yet we find that during thirteen months from March, 1914, to April, 1915, 3.95 per cent. of all admissions were cases of ascites. This was out of a total of 2250 admissions. Excluding all general surgical cases and eye, ear, nose, throat, and neurological patients, in whom there were no cases of ascites, we have left 452 patients admitted to the medical wards during a period of eight months. Of these 70, or 17.69 per cent., were suffering from ascites.

It must be borne in mind that the prevalence of any disease among the Chinese cannot be determined by hospital statistics. A large proportion of medical cases are never sent to an institution but are treated at home by an old-style Chinese physician. Surgery being an unknown art to these, a much larger percentage of surgical cases are sent to the practitioner of western medicine. The Chinese doctor stands helpless before a case of advanced ascites, while he believes that his decoctions will have a beneficial effect upon other medical conditions.

Nevertheless, it is our belief that those pathological processes which lead to the accumulation of free fluid in the abdomen are unusually prevalent among the Chinese of Canton and its environs, and it was with this in view that the present study was undertaken.

At the start it should be made clear that our data were collected under many difficulties. The histories are not always complete. Blood and urine examinations were omitted in some cases, and the modern procedures of electrocardiography and renal function tests could not be employed at all. A physical examination was made, however, in every patient, and upon this alone the diagnosis must rest in some. We are assured that free ascitic fluid was present in all the cases reported.

The present paper is based on data obtained from 80 patients, all of whom had ascites from some cause. Several were admitted to the hospital two or three times, and the period of residence varied from a few hours to several months. These 80 cases have been classified under eight heads, in accordance with the dominant pathological lesion, so far as it could be determined, without an autopsy. These eight groups are as follows:

| Predominant lesion. | Cases. | Percentage. |
|---|---|---|
| Hepatic disease | 22 | 27.5 |
| Splenomegaly | 13 | 16.25 |
| Hepatic disease and splenomegaly | 5 | 6.25 |
| Nephritis | 21 | 26.25 |
| Heart disease | 10 | 12.5 |
| Nephritis and heart disease | 3 | 3.75 |
| Tuberculous peritonitis | 4 | 5.0 |
| Abdominal tumors | 2 | 2.5 |
| Total | 80 | 100.0 |

The nationality of all these cases was Chinese. Only patients who were admitted to the wards are considered. For the present we shall confine our attention to the first six groups, leaving the tuberculous cases and the abdominal tumors for later study.

Differential Diagnosis. Of the 22 cases of hepatic disease there was definite clinical evidence of some pathological process in the liver in only 6, in which there was marked enlargement, local tenderness, or jaundice. The remaining cases were classified as hepatic disease, probably atrophic cirrhosis, because of the absence of definite signs of lesions in other organs that might produce ascites.

In 13 cases there was marked enlargement of the spleen without signs of liver involvement.

In 5 cases both spleen and liver were enlarged or there was splenomegaly with jaundice. Some of this group might fairly be classified as Banti's disease.

The 21 cases of nephritis were characterized by albuminuria or other signs suggesting chronic interstitial nephritis.

In 10 cases there was no definite abnormality in the urine, but there were present signs of endocarditis or myocarditis.

In 3 patients there was marked albuminuria associated with organic heart disease. Enlargement of the liver or spleen when it occurred in the cases classed as cardiac appeared to be the result of chronic passive congestion.

*Age.*

| | Under 20 years. | 20 to 39 years. | 40 to 60 years. |
|---|---|---|---|
| Hepatic | 2 | 10 | 10 |
| Splenomegaly | 0 | 9 | 4 |
| Hepatic and splenic | 0 | 4 | 1 |
| Nephritis | 2 | 15 | 4 |
| Cardiac | 0 | 5 | 5 |
| Cardiac nephritis | 0 | 3 | 0 |

All of the cases were between the ages of nineteen and sixty years except one child of three, with acute nephritis. The hepatic and cardiac cases showed about equal numbers before and after the fortieth year. There were more than four times as many cases of nephritis under forty years of age as over, indicating that this condition is more prone to affect young adults. Splenomegaly was also more common in the third and fourth decades than in the fifth

and sixth. Our series indicates that ascites is rarely found in the Chinese under nineteen years of age unless it be caused by tuberculous peritonitis.

*Sex.* Only 18 of the 80 cases were female. Of these 4 had tuberculous peritonitis or abdominal tumors, 1 splenomegaly, 4 cirrhosis of liver, 4 nephritis, 4 heart disease, and 1 cardiorenal disease. Excluding the cases of tuberculous peritonitis and abdominal tumors, 81 per cent. of the patients were males and 19 per cent. were females.

*Place of Birth.* Many patients came from towns and villages at a distance from Canton, but all but 6 came from the province of Kwangtung.

Nineteen men and four women were recorded as unmarried.

OCCUPATION OF SEVENTY CASES.

| Occupation. | Hepatic. | Splenic. | Hepatic-splenic. | Nephritic. | Cardiac. | Cardio-renal. | Totals. |
|---|---|---|---|---|---|---|---|
| Printer | .. | .. | .. | .. | 1 | .. | 1 |
| Student | .. | .. | .. | 1 | .. | .. | 1 |
| Farmer | 8 | 3 | 2 | 1 | 1 | 2 | 17 |
| Shopkeeper | 4 | 1 | .. | 4 | 2 | .. | 11 |
| Sailor | 1 | 2 | .. | .. | .. | .. | 3 |
| Soldier | 1 | 1 | .. | 3 | 1 | .. | 6 |
| Teacher | .. | .. | .. | 1 | 2 | .. | 3 |
| Gambler | .. | .. | 1 | .. | .. | .. | 1 |
| Laborer | 3 | 4 | 1 | 6 | 1 | 1 | 16 |
| Clerk | .. | .. | .. | 2 | .. | .. | 2 |
| Housework | 2 | .. | .. | 1 | .. | .. | 3 |
| Dressmaker | .. | .. | .. | .. | 2 | .. | 2 |
| Painter | 1 | .. | .. | .. | .. | .. | 1 |
| Weaver | .. | .. | 1 | .. | .. | .. | 1 |
| Cook | .. | 1 | .. | .. | .. | .. | 1 |
| Child (3 years) | .. | .. | .. | 1 | .. | .. | 1 |

The list of occupations throws but little light on the etiology of ascites. The great majority of patients admitted to the hospital are farmers, laborers, or shopkeepers. It is striking that most of the patients lived in the country and had spent but a few years at most in the city.

*Family History.* The family history was often unreliable and the causes of death of parents or other relatives were difficult to ascertain. One case of cirrhosis of the liver reported that his father died of dropsy. Of the splenomegaly cases the father of one died of edema and the sister of another died from the same cause. In a patient with enlarged spleen and liver the mother was reported to have died of heart disease. Four of the twenty-one nephritics reported a suggestive family history, and one of the cardiac cases stated that his mother died of edema. Thus in only 9 of the 74 patients could any definite family history bearing on the present disease be obtained.

*Previous Disease.* These records are not complete in regard to previous history. There were 9 who reported attacks of chills and fever, 4 had had dysentery. There is no doubt that malaria is an important factor in the causation of many cases of splenomegaly, but more especially cases not complicated with ascites. Dysentery was more frequently an initial symptom than a previous illness. The nephritis cases showed a tendency to relapse. Four had had previous attacks, each followed by temporary recovery. We have personally observed patients suffering from marked parenchymatous nephritis of the chronic type, in which all signs of disease, including albuminuria, have entirely disappeared. Twenty-nine out of 40 cases denied venereal infection, but a Wassermann test was not made, and undoubtedly more were infected.

ALCOHOL AND OPIUM. ALCOHOLISM IN 47 CASES OF ASCITES.

| | Hepatic. | Hepatic-splenic. | Splenomegaly. | Nephritis. | Cardiac. | Cardiorenal. |
|---|---|---|---|---|---|---|
| Total abstainer . . . | 0 | 0 | 1 | 1 | 1 | 1 |
| Takes less than 500 c.c. daily . . . . . | 9 | 4 | 3 | 9 | 3 | 2 |
| Takes more than 500 c.c. daily . . . . . | 4 | 0 | 2 | 2 | 5 | 0 |
| Percentage of cases using alcohol . . . . | 100.0 | 100.0 | 83.3 | 91.6 | 88.8 | 66.6 |

Alcohol is drunk as rice wine generally. This may vary in strength from 4 per cent. up. Drunkenness is rare, but drinking is practised pretty generally. Though we have no data on this subject in a number of cases studied, yet our table indicates that in cirrhosis of the liver, with ascites at least, alcohol is probably an etiological factor.

Only 5 of the patients were opium smokers. We cannot assign therefore any great importance to the use of this drug.

The mode of onset of the disease was determined by careful questioning in most cases. When disease of the liver or spleen was the underlying cause, abdominal enlargement was usually the first marked sign. In affections of the heart and kidney edema of the legs was generally the first thing noted. In 6 cases the disease was ushered in by an intitial attack of diarrhea or dysentery.

DURATION AND RESULT OF DISEASE.

| | Duration of illness before admission to hospital in 71 cases. | | | | | | Time spent in hospital in 74 cases. | | | | | | Result in 73 cases. | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Under 1 mo. | 1 to 2 mos. | 2 to 6 mos. | 6 mos. to 1 yr. | 1 to 2 yrs. | 2 to 15 yrs. | 1 to 7 days | 7 to 14 days. | 2 to 3 wks. | 3 to 4 wks. | 1 to 2 mos. | 2 to 4 mos. | Recovered. | Much improved | Improved. | Unimproved. | Death. |
| Hepatic . . . . . | 8 | 4 | 4 | 2 | 0 | 3 | 7 | 5 | 2 | 7 | 0 | 1 | 2 | 5 | 8 | 2 | 4 |
| Splenic . . . . . | 2 | 4 | 2 | 1 | 2 | 2 | 2 | 3 | 0 | 4 | 4 | 0 | 0 | 7 | 4 | 0 | 2 |
| Hepatic-splenic . . . . . | 0 | 2 | 1 | 0 | 0 | 2 | 1 | 0 | 2 | 1 | 1 | 0 | 0 | 1 | 2 | 1 | 1 |
| Renal . . . . . | 2 | 5 | 5 | 6 | 1 | 1 | 5 | 3 | 0 | 5 | 8 | 0 | 0 | 9 | 9 | 0 | 3 |
| Cardiac . . . . . | 2 | 2 | 4 | 1 | 0 | 0 | 2 | 4 | 1 | 2 | 0 | 1 | 1 | 4 | 2 | 0 | 3 |
| Cardiorenal . . . . . | 1 | 1 | 0 | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 1 | 0 | 0 | 2 |

It will be noted by examining the above table that many cases had been suffering for weeks or months before admission to the hospital. A few cases died a few days after admission, but the majority remained for one or more weeks, giving sufficient time for study and diagnosis. It may not be correct to speak of recovery in patients with ascites. However, 2 of the hepatic cases and 1 heart case left the hospital free of symptoms. The most satisfactory results were obtained in the renal cases. There was less tendency for the ascitic fluid to recur, although albuminuria generally persisted.

Unfortunately, no autopsies could be performed, but the cause of death was usually quite evident. Two of the hepatic cases that died were not tapped. One had a terminal enteritis and the other showed marked jaundice, and delirium. Another patient died of a probable abscess of the liver. Two with splenomegaly died. One of these became delirious soon after aspirating the fluid, and remained in this condition until death. The other, a young woman, from whom 15,000 c.c. of fluid were removed, died twelve hours later in collapse.

There were 2 cases of cirrhosis, or enlargement of the liver and splenomegaly, who died. In 1 case there was an abscess of the liver which ruptured into the lung. The other died shortly after leaving the hospital with symptoms of cerebral embolism which followed aspiration.

One of the cases of nephritis became uremic after the second aspiration and died.

Of the patients with heart disease 1 died with signs of cerebral embolism which came on soon after tapping the abdomen. One who was not tapped showed signs of beriberi. The third heart case, who had aortic incompetency, died soon after aspiration.

Two patients with advanced heart and kidney disease died. One showed marked jaundice and toxemia and the other died of advanced mitral disease with decompensation.

*Temperature.* A normal or subnormal temperature was usual. There were 18 cases in whom the thermometer reached as high as 100°. In 7 cases it reached 101°. In 4 cases it rose to 102° or above.

Twenty-six of the case histories gave no record of the condition of the heart. It may be assumed that in these there was no heart disease or at most a functional impairment.

In 3 of the patients with splenomegaly a mitral systolic murmur was heard, probably functional. In 5 of the patients with nephritis there were signs of heart disease, but the renal symptoms were decidedly predominant.

There were 10 cases, however, in which the ascites was considered as a complication of organic heart disease. Seven of these showed mitral regurgitation, 2 aortic regurgitation, and 1 evidence of myocarditis.

## THE CIRCULATION.

| | Condition of heart. | | | | | | | | | Rate of pulse. | | | | | | | | | | Blood-pressure (systolic). | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Normal. | Mitral diastolic. | Mitral systolic. | Aortic diastolic. | Tricuspid systolic. | Hemic murmur. | Accentuation of 2d aortic. | Feeble. | No record. | 120 | 110 | 100 | 95 | 90 | 80 | 75 | 70 | 65 | 55 | No record. | 225–238 | 200 | 180 | 170 | 150 | 130 | 120 | 115 | 110 | 100 | 80 | 60 | No record. |
| Hepatic | 7 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 15 | 3 | .. | 4 | .. | 3 | 7 | 2 | 0 | .. | .. | 3 | .. | .. | .. | .. | .. | .. | 2 | .. | 2 | 1 | .. | .. | 17 |
| Splenic | 5 | 0 | 3 | 0 | 0 | 0 | 0 | 1 | 4 | .. | .. | .. | .. | .. | 6 | 1 | 1 | .. | 1 | 4 | .. | .. | .. | .. | .. | 2 | .. | 2 | 1 | .. | .. | .. | 8 |
| Hepatic and splenic | 4 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | .. | .. | 1 | .. | .. | 3 | .. | 1 | .. | .. | 0 | .. | .. | .. | .. | .. | .. | 1 | .. | 1 | 2 | .. | .. | 1 |
| Renal | 7 | 1 | 3 | 0 | 1 | 0 | 1 | 1 | 7 | .. | .. | 2 | 1 | 5 | 7 | .. | 1 | 1 | .. | 4 | .. | 1 | 1 | 2 | 1 | 1 | 1 | 2 | .. | .. | .. | 2 | 10 |
| Cardiac | 0 | 0 | 7 | 2 | 0 | 0 | 0 | 1 | 0 | .. | 1 | .. | .. | 2 | 5 | .. | 1 | .. | .. | 1 | 1 | .. | .. | .. | 1 | 2 | 2 | .. | .. | 2 | 1 | .. | 1 |
| Cardiorenal | 0 | 0 | 2 | 0 | 0 | 1 | 0 | 0 | 0 | .. | .. | 1 | .. | .. | .. | .. | 0 | .. | .. | 2 | .. | .. | .. | .. | .. | .. | 1 | 1 | .. | .. | .. | .. | 1 |

Out of 452 patients admitted to the medical wards of the hospital in 1914, 19 were diagnosed as heart disease, and 5 of these, or 26.3 per cent., had ascites.

The pulse-rate was not generally increased above 80. Excessive accumulation of ascitic fluid caused embarrassment of the heart and a consequent acceleration of the pulse.

The systolic blood-pressure was estimated in several cases. The Nicholson apparatus was used. The highest reading was found in a case of aortic regurgitation.

In general, aspiration of fluid has no appreciable effect on high pressure. There might be a temporary fall, but the next day it returned to the original reading; except in one instance of aortic regurgitation the higher readings were found in cases of nephritis.

HEMOGLOBIN IN THIRTY-FOUR CASES.

| | 90 to 100 per cent. | 80 to 89 per cent. | 70 to 79 per cent. | 60 to 69 per cent. | 50 to 59 per cent. | 20 to 29 per cent. |
|---|---|---|---|---|---|---|
| Hepatic | .. | 1 | 2 | 1 | | |
| Splenic | .. | 2 | 3 | | | |
| Hepatic and splenic | 1 | 3 | | | | |
| Renal | 1 | 2 | 3 | 4 | 2 | 1 |
| Cardial | .. | 2 | 3 | 1 | | |
| Cardiorenal | .. | 2 | | | | |

Anemia is especially marked in the nephritic cases, more than half of which were below 70 per cent.

*Respiratory System.* The records of the lungs and respiratory organs were not complete. There was no case of pneumonia. In the majority of patients there was marked dyspnea on admission because of the intra-abdominal pressure. This usually soon disappeared after aspiration. In only 4 was there evidence of pleural effusion: three on the left and one on the right side. The effusions were moderate and did not require tapping.

*Liver.* Enlargement of the liver was noted in 7 cases. In 2 there was tenderness, but in only 1 was an abscess demonstrated. In this last case the pus discharged into the lungs. There was a marked infection of clonorchis sinensis. In several instances it was not definitely stated whether the liver was enlarged or not. It is probable that in most of these it was of normal size or reduced.

*Spleen.* The spleen was noted as enlarged in 19 cases, in 1 of which the enlargement was apparently caused by passive congestion. Excluding this there were only 18 cases, or 24 per cent., with splenomegaly; 4 of these cases appeared to be Banti's disease. Among the others 1 was diagnosed cancer of the spleen, in 3 there was a history of malaria, and in 1 of excessive alcoholism. The spleen did not average as large as in many cases of splenomegaly without ascites.

*Digestive System.* Pressure of the fluid on the stomach and intestines always caused marked digestive disturbance. Severe

enteritis was a frequent complication. In 1 patient with nephritis and marked albuminuria, suppression of urine was difficult to overcome until a violent acute enteritis developed, when the urinary output was markedly increased.

OVA OF INTESTINAL PARASITES.

| | No record. | No ova. | Ankylostoma. | Ascaris. | Trichocephalus. | Ascaris, ankylostoma, trichocephalus. | Ascaris, clonorchis sinensis. | Clonorchis sinensis. | Clonorchis trichocephalus. | Clonorchis ankylostoma. |
|---|---|---|---|---|---|---|---|---|---|---|
| Hepatic | 16 | 4 | .. | 1 | 1 | .. | .. | .. | .. | .. |
| Splenomegaly | 6 | 3 | 2 | 1 | .. | .. | 1 | .. | .. | .. |
| Hepatic and splenomegaly | 1 | 1 | .. | .. | 1 | .. | .. | .. | .. | .. |
| Renal | 9 | 4 | 1 | 3 | 2 | .. | .. | 1 | 1 | 2 |
| Cardiac | 2 | 7 | .. | .. | .. | .. | 1 | .. | .. | .. |
| Cardiorenal | .. | .. | 1 | .. | 1 | 1 | .. | .. | .. | .. |

It is to be regretted that the feces were not examined in all of the patients. There were 40, however, in whom ova were looked for and there was evidence of parasites in about one-half of these. Ankylostoma and clonorchis sinensis by their own pathological processes producing either a profound anemia on the one hand or extensive disease of the liver on the other, may be directly responsible for the ascites. Hookworms were present in 7 cases while clonorchis was found in 6. In 2 of the latter there was great abundance of ova in the feces, and there was marked tenderness over the liver.

*The Urine.* In all patients in whom albuminuria was marked a diagnosis of nephritis was made. In 2 cases there were signs of chronic interstitial nephritis, but no albumin was found in the urine. In 15 cases with nephritis there was a heavy precipitate of albumin, the amounts varying from 0.5 gm. to 10 gms. excreted per 1000 c.c. of urine. Granular and hyaline casts were generally found in these cases.

Ascites resulting from Bright's disease is almost always associated with marked albuminuria. The urine is often very scanty, only 100 c.c. to 500 c.c. being voided in the twenty-four hours. It was observed that in favorable cases the disease appeared to remain stationary for a time until a crisis, so to speak, occurred, when the urine increased in quantity and ascitic fluid ceased to accumulate in the abdomen. This critical change was brought about in some cases after the first or second tapping, in other instances the improvement took place some days or weeks after removing the ascitic fluid. In unfavorable cases retention of urine and symptoms of uremia followed soon after the aspiration of the abdominal fluid.

In the hospital report for 1914 there appear but 32 cases of nephritis, and according to our series 21 of these showed more or less ascitic fluid.

EDEMA RECORDED IN SIXTY CASES.

| | None. | Legs and feet only. | Feet and scrotum. | Face and feet. | General anasarca. |
|---|---|---|---|---|---|
| Hepatic | 3 | 9 | 2 | .. | 1 |
| Splenomegaly | 5 | 4 | 0 | | |
| Hepatic and splenomegaly | 2 | 2 | 0 | | |
| Renal | .. | 3 | 3 | 1 | 12 |
| Cardiac | .. | 6 | .. | .. | 4 |
| Cardiorenal | 1 | 1 | 1 | | |

It is very evident from the above table that in cases of nephritis ascites is likely to be part of a general anasarca. When edema appeared in cases of cirrhosis of the liver or splenomegaly it was usually caused by pressure on the lower extremities and was soon relieved by removing the cause.

In the heart and kidney cases this was not so generally the case. If a free flow of urine was not established by tapping the edema persisted or quickly returned.

If the edema disappeared in renal cases after aspirating the abdomen a favorable prognosis was justifiable, but if the edema persisted there was little prospect of recovery.

The frequent occurrence of edema in cases of nephritis among the Chinese is of special interest because of recent studies of the effect of sodium chloride on this disease. It is well known that the best method of treating the edema of Bright's disease is by giving a diet free of salt. Now, salt among the Chinese is a luxury seldom indulged in by the lower classes. Rice, the main diet, is cooked and eaten without any salt. Meat is eaten in very minute portions by the laborer, and vegetables are likewise prepared without salt. We have, therefore, to do with a people who rarely eat salt and whose diet is almost purely vegetarian, and yet afflicted with a severe form of nephritis frequently accompanied by local edema, ascites, or general anasarca. In this connection it is also of interest to note that the dairy products—milk, butter, and cheese—do not form part of the dietary of the average Chinese.

Ascites caused by disease of the heart and kidneys is often relieved by appropriate treatment of these organs and the fluid does not have to be withdrawn so often as in patients suffering from cirrhosis of the liver or splenic enlargement. In 2 of the hepatic cases in whom the fluid was not withdrawn there was a large amount present, but the patients being *in extremis* no operative procedure was ventured upon. The largest amount of fluid was found in 2 cases of cirrhosis, in 1 of which 20 liters and in the other 16½ liters were removed at the first tapping. It was generally found necessary to aspirate when the fluid reached between 5 and 10 liters. Less than this amount caused comparatively slight discomfort, and more produced much oppression with nausea and vomiting.

Many cases are reported as being tapped but once, but in some cases there was a gradual reaccumulation of fluid. In only 4 was there no tendency to recurrence after tapping. In 9 the fluid was

DATA REGARDING ASCITIC FLUID IN SEVENTY-FOUR PATIENTS.

| | Not aspirated. | Spontaneous disappearance. | No tendency to recur after tapping. | Number of times aspirated. | | | | | | | Average amount of fluid when tapped more than once. | | | Maximum amount of fluid drawn at one time. | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Once. | Twice. | Three times. | Four times. | Five times. | Six times. | Times not recorded. | 5000 c.c. or less. | 5000 to 10,000 c.c. | 10,000 to 20,000 c.c. | Under 1000 c.c. | 2000 c.c. | 3000 c.c. | 4000 c.c. | 5000 to 10,000 c.c. | 10,000 to 15,000 c.c. | 15,000 to 20,000 c.c. |
| Splenomegaly | 2 | 2 | .. | 5 | 3 | 2 | .. | .. | .. | 1 | .. | 4 | .. | .. | .. | .. | 1 | 6 | 2 | |
| Hepatic and splenomegaly | .. | .. | .. | 3 | .. | .. | .. | .. | 1 | 1 | .. | 1 | .. | .. | 1 | .. | 1 | 1 | | |
| Renal | 5 | 4 | 1 | 6 | 7 | 1 | 1 | .. | .. | 1 | 1 | 5 | 1 | .. | 1 | 1 | .. | 8 | 3 | |
| Cardiac | 4 | 3 | 2 | 4 | 1 | .. | 1 | .. | .. | 2 | .. | 2 | .. | 1 | .. | 1 | 1 | 2 | 1 | |
| Cardiorenal | .. | .. | .. | 1 | .. | .. | .. | 2 | .. | 1 | 1 | 1 | .. | .. | .. | .. | 2 | 1 | | |
| Hepatic | 3 | .. | 2 | 8 | 4 | .. | 1 | .. | .. | 6 | 1 | 1 | 2 | .. | .. | .. | 3 | 2 | 2 | 2 |

gradually absorbed, but in these there was at no time a very large amount.

TREATMENT. Diuretic drugs had little effect. When large amounts of ascitic fluid were present no relief was obtained until this was drawn off. The urinary output then increased and edema rapidly disappeared. Compound jalap powder proved to be the most satisfactory purgative. Little benefit was derived from hot sweat baths. Unfortunately due attention was not paid to the dietetic treatment of these cases.

TUBERCULOUS CASES. There were 4 patients with tuberculous peritonitis and ascites. Two were in children aged about fourteen, a boy and a girl, and two in adults, a man aged twenty-three and a woman forty-three. In three the abdominal distention was the primary condition with chills and fever. The woman gave a history of a long-standing pulmonary lesion. Abdominal section was performed in two. One, a child, was improved. The man of twenty-three was operated upon because of the very rapid accumulation of fluid. Only temporary relief was afforded, and he died on the sixteenth day after admission. All of these 4 cases ran a febrile course with rapid pulse. In the two adults tubercle bacilli were found in the sputum. Edema was absent or very slight.

PELVIC TUMORS. In two women ascites was associated with tumors of the genitalia. From one 4000 c.c. of clear fluid were aspirated before the diagnosis was made. The liver was enlarged. Operation was refused. The other case was a widow, aged forty-one years. On admission 10 liters of dark brown fluid were withdrawn, containing many cholesterin crystals. Upon abdominal section, later, an extensive carcinomatous growth was found, involving tubes, ovaries, and the peritoneum. A panhysterectomy was performed. Patient made a good recovery and was discharged from the hospital well after four months.

CONCLUSIONS. 1. Ascites is a common condition in the medical wards of a hospital in Canton.

2. This condition is most frequently associated with cirrhosis of the liver or chronic nephritis, but splenomegaly, heart disease, tuberculous peritonitis, and abdominal tumors are also causative factors.

3. The male sex is more prone to this form of disease than the female, and most cases occur between the twentieth and sixtieth years.

4. The majority of cases with ascites give an alcoholic history.

5. Although the Chinese are largely vegetarian in their diet, and seldom eat salt, nephritis associated with edema is by no means uncommon.

6. Ascitic fluid tends to recur after tapping, especially in cases of cirrhosis of the liver and splenomegaly. The best results were obtained when the ascites was caused by heart or kidney disease.

# REVIEWS

LIFE OF DR. LYMAN SPALDING. By DR. JAMES ALFRED SPALDING. Pp. 367. Boston: W. M. Leonard, 1916.

THE author, a grandson of the subject of the biography, came within recent years upon a collection of papers, chiefly of letters, left by his grandfather, who lived from 1775 to 1821. They are, indeed, "a treasure for illuminating American medical history" of this early period, and this biography well deserves a place of honor in the libraries of medical men. Lyman Spalding was a protege and later a colleague of the famous Nathan Smith, the surgeon, who founded the Dartmouth Medical School, and father of the more famous surgeon, Nathan R. Smith. Dr. Spalding graduated from the Harvard Medical School in 1797, then taught chemistry for two years in the new Dartmouth Medical School, practised thirteen years in Portsmouth, N. H., spent one year (1809–1810) attending medical lectures in Philadelphia, lectured on anatomy and surgery in and was president of the Medical School in Fairfield, N. Y., for two years (1810 to 1812), and practised four years in New York. He played an important part in the introduction of vaccination into this country, and was the first physician in the country to read a paper on a National Pharmacopœia and to offer a working basis for its foundation. Although a committee was appointed to carry out his idea, he did nearly all the work personally, and carried the book through to its publication and sale. He developed a wide acquaintance among the most prominent members of the profession of his time, especially in this country, but also in England and France, and his numerous letters from these men come now as a very valuable contribution to the history of early American medicine. H. D.

ANATOMICAL NAMES. By A. C. EYCLESHYMER, Head of Department of Anatomy of the University of Illinois. Pp. 774. New York: William Wood & Co., 1917.

THE value of the work done by the German Commissions appointed in 1887 to simplify the terms employed in the science of anatomy is now well established, and its name, the "Basle Nomina Anatomica,"

or its official abbreviation, BNA, needs no explanation. To maintain a familiarity with the recent anatomical literature we must be familiar with this system. The author, with the aid of D. M. Schoemaker, professor of Anatomy, of St. Louis University, presents the system with an English translation of the Commission's report, adopted more than twenty years ago. There is added a collection of some twenty thousand synonyms, each of which bears numerals citing the equivalent BNA term. There also has been included a biographical list, containing some eight hundred brief sketches of the leading anatomists of the whole world, which was prepared by Roy L. Moodie, assistant professor of anatomy of the University of Illinois. English anatomists and all those interested in the modern literature of anatomy will appreciate the value of this aid in their work.

T. T. T.

DISEASES OF CHILDREN. By GEORGE M. TUTTLE, M.D., Clinical Professor of Pediatrics, Washington University, St. Louis, and PHELPS G. HURFORD, Assistant in Pediatrics, Washington University, St. Louis. Third edition. Pp. 584; 47 engravings and 4 plates. Philadelphia: Lea & Febiger, 1917.

THIS volume is more properly a manual of the diseases of children, extremely concise, compact, very well arranged, and classified. The authors have, in this edition, thoroughly revised the former views, incorporated new scientific investigations from the literature and added much from personal and hospital observations.

It is more practical than a scientific text-book. A handy and ready reference book for both student and practitioner.

J. D.

TRAUMATIC SURGERY. By JOHN J. MOORHEAD, B.S., M.D., F.A.C.S., Adjunct Professor of Surgery, New York Post-Graduate Medical School and Hospital. Pp. 736. 522 illustrations. Philadelphia and London: W. B. Saunders Company, 1917.

THE presentation of a book devoted to traumatic surgery is opportune at this time because of the increased claims for damages under the compensation laws and the requirements of war surgery, so much of which is to be done by general practitioners who have not had special training for this work. The book is purposely didactic and follows the course of clinical lectures given by the author. The injuries of the various parts and tissues of the body are considered.

Arthroplasty as practised by the late John B. Murphy is strongly presented by a series of excellent illustrations. The three illustrations of the operation of reefing the capsule for recurrent dislocations of the shoulder-joint are not so valuable and will mislead the surgeon who is led to try this operation. They show an impossible exposure of capsule, ignore the important overlying rotator muscles, and show the external rotators attaching to the humerus below the surgical neck, whereas the capsule attaches to the anatomical neck above the tuberosities, which are consequently below and outside the joint. To limit the phases of trauma to be discussed is not a simple task, especially with reference to its late and indirect effects. The author has aimed to present information necessary for the diagnosis and treatment of all the usual and most of the unusual effects of accident and injury. A chapter is given to the eye and ear examinations of railway and other employees and another to medicolegal phases.

T. T. T.

# PROGRESS
OF
# MEDICAL SCIENCE

## MEDICINE

UNDER THE CHARGE OF

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**A New Instrument for Percussion and Auscultation.**—In the continual struggle for accuracy in methods of physical diagnosis, TORNAI (*Wien. klin. Wchnschr.*, 1916, xxix, 1625) describes an instrument which he considers a distinct advance in the field of auscultation and percussion. It is a modification of an earlier apparatus which he described in connection with "phonoscopic percussion" in 1912, and which he called at that time the "phonoscope." The new instrument is called the "novoscope," and consists essentially of a single-stemmed stethoscope bell or chest piece connected by a short piece of stethoscope tubing to a metal Y tube, the two arms of the Y being connected with the ears by rubber tubing and vulcanite olives, or by tubing and the ordinary metal stethoscope ear pieces. The metal Y is connected to a metal head piece, such as is used with head mirrors, by means of an aluminum rod, which has a joint in its center permitting movement of the distal half of the rod upward through 180° in the vertical plane. The connection of the rod to the head band is made by a ball and socket joint which can be locked by a thumbscrew. With the head piece adjusted and the ear pieces in position, locking the ball and socket joint with the rod extended in front of the examiner's head permits him to percuss, with the stethoscope bell just above the percussing fingers, and the examiner listens to the percussion sounds through the medium of the stethoscope. Loosening of the ball and socket joint on the head piece converts the instrument into an easily usable stethoscope for auscultation. The writer contends that percussion tones are heard much better by this method, which enables

finer distinctions to be made in the pitch and quality of the percussion notes, so that greater accuracy is secured in the percussion of the chest and its contents. He states that very light percussion strokes must be used—preferably the so-called "threshold percussion"—and the patient examined in a very quiet room. The results obtained by this method of percussion in his hands are exceedingly accurate. The instrument is small and can be folded to carry in the pocket, and is so simple in design that any clever mechanic can construct one in a very short time.

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**Diminished Blood Platelets and Marrow Insufficiency.**—Minot (*Arch. Int. Med.*, 1917, xix, No. 6, p. 1062) discusses at length the findings in a series of cases of purpura hemorrhagica and aplastic anemia. The two conditions are often confused, and in most text-books no differential diagnosis between the two conditions is mentioned. There is also often much confusion between the chronic types of purpura hemorrhagica and hemophilia, this confusion usually arising from incomplete studies of the blood in these cases. Minot's conclusions were derived from the literature (of which he presents an extensive bibliography) and from the study of some 25 cases in the purpura hemorrhagica and aplastic anemia groups. Purpura hemorrhagica is a condition in which there is bleeding from one or more mucous membranes, often purpuric skin lesions, associated with diminished blood platelets, a delayed bleeding time, and a soft non-retractile blood clot. The coagulation time is normal or slightly delayed, rarely much delayed. The condition is more usually secondary to some recognized disease, as diphtheria or tuberculosis, and is also to be considered secondary when it appears as a symptom accompanying aplastic anemia, leukemia, bone-marrow tumors, pernicious or splenic anemia, etc. When no recognized cause can be found for its presence it is then spoken of as a disease entity—purpura hemorrhagica or Werlhof's disease. Idiopathic purpura hemorrhagica may be a disease that is acute, subacute, chronic or of an intermittent nature. A congenital and hereditary type exists. Acute aplastic anemia is a disease of unknown etiology which runs a progressively downward, fatal course of three to six weeks' duration. It occurs usually in patients between fifteen and thirty years of age. Fever frequently occurs, and there is no evidence of increased blood destruction as in pernicious anemia. It seems that whatever the cause of the disease may be its action is to inhibit the activity of the blood forming elements in the bone marrow, for at autopsy the marrow is found to be completely fatty. Near the termination of pernicious anemia, and in the course of certain infections, as sepsis, malignant endocarditis, typhoid fever, diphtheria, miliary tuberculosis, etc., aplasia or exhaustion of marrow may occur. In such instances we speak of a secondary aplastic anemia, the only difference between this form and the idiopathic aplastic anemia being that in the first type we recognize a source for the toxin formation and in the second we do not. In aplastic anemia the blood picture shows no evidence, or very little, of regeneration of the red cells, platelets or polynuclear leukocytes. The red cells may be very low in number (often 500,000 before death), and yet the color index averages 0.8 or slightly higher, and there is little or no variation in shape and very little variation in size. Polychromatophilia, stippling, blasts,

reticulated red cells and Howell-Jolly bodies are absent or rare. If the color index is high, and there is an occasional and unduly large and especially an oval shaped erythrocyte found, with all the other characteristics of an aplastic anemia, the suspicion that the case was one in which an aplasia of the bone marrow had developed in the course of pernicious anemia is warranted. The platelets in aplastic anemia are markedly diminished in number, often nearly absent, and they vary in size in different cases. The white cells are diminished in number, more so as the disease progresses. The leukopenia consists in an absolute diminution in the number of polynuclear cells and usually disappearance of the eosinophiles, with thus a relative but not an absolute increase in the lymphocytes, the percentage of lymphocytes averaging 73 per cent. These cells are of the normal type. There is usually a "shift to the left" (Arneth) in the polynuclear types contrasted with the frequent "right handed shift" pointed out in pernicious anemia by Briggs. The only distinctive feature of the blood picture in purpura hemorrhagica is the marked decrease in the number of blood platelets. The blood picture in this disease is therefore one consistent with a bone marrow which is incapable of forming platelets, but competent to a greater or less degree to produce polynuclears and red cells. The anemia in these cases is due to the hemorrhages and not apparently to any lack of formation or increased destruction of red cells. The red cells then are of the type usually found in an acute or chronic posthemorrhagic anemia—variation in size evident in shape, slight, some achromia occurs, and the color index is usually lowered. Polychromatophilia and stippling occur, occasionally a few normoblasts, and rarely a Howel-Jolly body. Reticulated red cells are increased when definite anemia is present. The white cells are usually increased, usually about 12,000 and sometimes higher, with an increased percentage of polynuclear elements in the higher, and often in the lower counts. There seems to be a slight "left-handed shift" (Arneth) in the types of polynuclears. The platelets are diminished often as low as 1000. The normal count is 225,000 to 325,000. When the platelets are decreased below 60,000 hemorrhages tend to occur. This decrease in platelets is in marked contrast to the increase, frequently to 1,000,000, seen in ordinary posthemorrhagic anemias in which the picture is one of active bone marrow regeneration of all three of the formed elements. The platelets usually vary greatly in size being both abnormally small, and abnormally large. There are also cases which present blood pictures intermediate between these two groups, and which suggest that in them some agent is at work interfering unequally with the production of the formed elements. Such cases are those of purpura hemorrhagica which show no increased white count or a leukopenia, or a normal or slightly increased white count with a moderate increase in lymphocytes (50 per cent.). Other cases show chronic anemia without evidence of blood destruction and little hemorrhage, red cells suggestive of poor erythrocytic activity of the marrow, leukopenia with slight relative and absolute decrease of the polynuclears, and somewhat diminished platelet counts. These cases suggest a stage midway between purpura hemorrhagica and aplastic anemia. There are also cases in which the picture is that of an aplastic anemia, and yet in which the red cells show evidence of regeneration and the leukopenia and decrease in platelet count are not marked. These intermediate

cases seem related to the more clearly cut disease known as idiopathic purpura hemorrhagica because in common with it the nature of the disease process is unknown, the most marked symptom is purpura, and the most striking blood finding is the diminution in blood platelets. The data suggest that all these conditions with diminished platelets and purpura are similar, whether the marrow only is involved or whether there is increased platelet destruction in the plasma. The stimulation of the marrow in these cases offers the greatest hope in their treatment, and this is best done by transfusion. The study of the absolute and relative numbers of the polynuclears, the reticulated red cells and the platelets is the most satisfactory way of determining bone marrow activity. Needless to say, in asplastic anemia there is no evidence of bone marrow activity following transfusion, but in some cases of purpura hemorrhagica all of the formed elements may be favorably affected after transfusion, and in other cases only the red cells and polynuclears. In the intermediate cases the beneficial effects of transfusion upon the red and white cell production may be very slight, suggesting a partial aplasia of these marrow elements. The studies of the bone marrow in idiopathic purpura hemorrhagica have been rather few, and Minot reports an increase of the number of megakaryocytes in the marrow of a boy, aged fourteen years, who died from idiopathic purpura. The platelets may be reduced in the peripheral blood by destruction of the megakaryocytes of the bone marrow, by some toxin which inhibits the formation of platelets by the megakaryocytes or by destruction of the platelets in the peripheral circulation. It may possibly be that rapid destruction of platelets in the peripheral circulation causes in some cases, a depression of the whole marrow. In the aplastic anemias the reduction of platelets is due to diminution of the megakaryocytes just as the decreased red count is due to diminution in the red and white cell elements of the marrow. In certain of these cases presenting the blood picture of aplastic anemia the marrow may show areas of aplasia and areas of hyperplasia. These cases are really ones of incomplete aplasia and many cases terminating as complete aplasias show early in their courses a few regenerative red cells, produced by foci of still active marrow attempting to repair the destructive process. In the symptomatic cases of purpura hemorrhagica appearing in leukemia or tumor infiltrations of the marrow the megakaryocytes have been displaced by the new cells, so that they are decreased in number. In aplastic anemia it is reasonable to assume that some factor attacks the whole marrow, the red cell elements being inolved first and the platelets later as evidenced by the hemorrhage appearing after the anemia, while in purpura hemorrhagica the platelets are attacked first so that hemorrhages appear before the anemia which is largely referable to the loss of blood. In the cases intermediate between purpura hemorrhagica and aplastic anemia the "toxin" is probably such that, besides injuring the activity of the megakaryocytes, it impairs the function of either or both of the red and white cell elements of the marrow. In chronic diseases where depression of the marrow exists, there seems to be no "toxin" at work, but possibly a congenital peculiarity of the blood forming elements of the marrow, or a supernormal sensitivity to some toxin that ordinarily produces no such effect. It is also conceivable that disease of some other organ such as

the spleen may cause depression or inactivity of the bone marrow, just as disease of one of the glands of internal secretion may depress one of the others. The author then discusses the differential diagnosis of purpura hemorrhagica and aplastic anemia, pointing out that drug purpuras Henoch's purpura and Schoenlein's disease are not true purpura hemorrhagica. Purpura hemorrhagica and aplastic anemia must not be confused with hemophilia, the non-leukemic phase of leukemia, bone marrow tumors, pernicious anemia and splenic anemia. The distinguishing characteristics of hemophilia are the normal platelet count, blood clot and bleeding time, with the greatly delayed coagulation time; of the non-leukemic phase of leukemia, the picture of active regeneration of the red cells and polynuclears, the presence of abnormal forms of lymphocytes, and swelling of the lymph nodes; of bone marrow tumors, the history, physical examination, roentgen-ray findings (Bruce Jones protein in the urine in myeloma) and presence of abnormal cells, plasma cells or tumor cells should they occur in the peripheral blood; of pernicious anemia after aplasia of the marrow has occurred, the history of remissions, sore tongue and spinal involvement, color of the skin, and a high color index of the red cells with the presence of occasional large and abnormally shaped red cells; of splenic anemia, rather marked enlargement of spleen and later of the liver, though this disease is often difficult to distinguish from purpura hemorrhagica. The author gives a short classification of the types of purpura hemorrhagica and aplastic anemia and suggests that, instead of calling a group of disease conditions "purpura hemorrhagica," we use more specific terms and referred to cases of "insufficiency of the marrow with especial involvement of the platelets or other formed elements in varying degrees."

## SURGERY

UNDER THE CHARGE OF

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**Treatment of Gunshot Wounds of the Abdomen, with a Summary of 500 Cases seen in an Advanced Casualty Clearing Station.**—LOCKWOOD, KENNEDY and MACFIE (*British Med. Jour.*, March 10, 1917, p. 317) say that the earlier the patient could be operated on the better were the results. As late as twenty hours after being wounded, operation was considered the best course, and their results justified them. Judgment in cases seen after twenty to thirty hours presented much greater difficulties; there was always the danger of increasing the damage by manipulation during the operation. If general plastic peritonitis had developed, interference was not only valueless but dangerous; they were content to insert a pelvic drain, or, if a fecal fistula was found, to mop it out carefully and drain.

A few cases were operated on after thirty hours, but usually to drain a fecal collection. Autopsy was performed in some 80 per cent. of the cases which ended fatally without operation having been attempted; hemorrhage was found as the commonest cause of death. Shock accounted for most of the deaths within the first twenty-four hours after operation. General peritonitis was rare in cases operated on not later than twelve hours after being wounded, but later than that it was present in about 50 per cent. of deaths. Gas gangrene, especially of the posterior abdominal wall, was the cause of death in at least 30 per cent. of the cases. After nephrectomy and splenectomy death from embolism and infarct occurred in a small percentage of cases. In about 8 per cent. of cases operated on wounds of other parts of the body caused death. Of the 500 cases 356 were operated on and 144 were not operated on. The following conclusions were drawn: wounds of the large vessels to the liver, kidney, and spleen are fatal before they can come to operation. Wounds involving the pancreas are seldom seen on the operating table, by reason, perhaps, of the contiguity of the organ to large vessels; only one case was seen. In that the foreign body was lodged in the tail of the pancreas. Anteroposterior wounds, especially in the epigastrium, are least dangerous, and wounds from side to side, especially low down, are dangerous. Wounds of solid viscera are not so dangerous as those of hollow viscera. Cases that come to operation with a herniated loop of bowel exposed do badly, especially if much bowel is lying exposed; the same is true when the stomach is partially herniated. Wounds of the stomach, colon and especially the small intestine, require exploration, but in a posterior wound involving the colon the greatest care should be taken not to convert a retroperitoneal condition into an intraperitoneal one. Wounds of the liver and kidney should be carefully determined as such only, and then treated expectantly, doing no more than exploring and cleaning up the track, and not that if probably a through and through wound produced by an undistorted rifle bullet or shrapnell ball. Avoid resection. End-to-end anastomosis is preferable to lateral when resection is essential. Wounds of the diaphragm are not necessarily fatal, nor even to be greatly feared. Careful repair gives excellent results. Multiple drainage tubes are rarely necessary, and always to be avoided if possible. Abdominal lavage is a dangerous practice. Never leave free, unprotected gauze in the abdomen. Paul's tube should be relegated to the museum, except in very rare cases. Speed in operating is essential, not only for the benefit of the patient, but because of the demands of scores of less vitally wounded me requiring attention during an active offensive. Resection for fecal fistula is better done late when the patient is in England.

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**Direct Transfusion of Blood, with a Description of a Simple Method.**—FULLERTON and DREYER (*Lancet*, May 12, 1917, p. 715) say that treatment by direct transfusion of blood has attracted much attention of late during the course of the war, since benefit has been derived from it in many cases of hemorrhage and in certain cases of anemia secondary to sepsis. Lives have been saved when all other methods of resuscitation have failed. In many cases the effect has been immediate and dramatic. They have seen patients who were blanched and shocked and with pulse hardly perceptible brought back to life in a most astonishing way.

At the same time they do not recommend its indiscriminate use, and they have only resorted to it in cases which they considered desperate. Transfusion is effected from a small artery to a suitable vein. The apparatus used consists of two glass or silver cannulæ connected by a short length (about 7 inches) of India-rubber tubing, the whole being coated within and without by a thin layer of wax made by mixing hard and soft paraffin, in about equal parts. They use thin-walled, transparent, India-rubber tubing which will stand heat and which will allow pulsations to be easily felt during the operation. The cannulæ they have found most useful are made of silver with a bulbous end so as to ensure their retention in the vessels without the necessity of tying or holding them in. Glass cannulæ of similar size and shape may be used. The ends of these are bevelled by grinding on stone or brick to facilitate introduction. They have the advantage of being easily improvised in any ordinary clinical laboratory, but it is difficult to make a bulb of suitable size to fit tightly into the vessels, and they, therefore, require to be tied in or held—a most tiresome process. The dimensions of the cannulæ are as follows: Arterial cannula: length, 4 cm.; external diameter at point, 3 mm. The operation is done under local anesthesia. The radial artery of the donor was found most suitable, and one of the veins of the elbow or the internal saphenous of the recipient. When the two vessels to be employed are exposed they are ligated at their distal ends and a light bull dog forceps is placed on the proximal end of each. A V-shaped incision is then made with sharp scissors into each vessel. The introduction of the cannula is facilitated by making the incision in the vessel close to the ligature and seizing the flap thus made at its extremity with a fine forceps. The opening is thus made to gape. An analysis of the 16 cases transfused by this method shows that 1 received no blood owing to an undetected obliteration of the receiving vein. In 3 the patients appeared beyond hope of recovery and transfusion was only undertaken as a last resort. Of the other 12 in which improvement might have been anticipated, 4 made rapid and very satisfactory progress, which is attributed, without hesitation, to transfusion. In another case the recovery was not attributed to the transfusion. The remaining 7 cases died although hopes of their recovery were entertained. The fact that improvement took place in most of the cases that died encourages the belief that under similar circumstances in future transfusion might just tide the patient over a critical period and allow time and opportunity for further surgical treatment. Three cases transfused by this method by two other surgeons gave excellent recoveries.

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**Influence of the Venous Collateral Circulation of the Kidney on Hydronephrosis.**—Barney (*Ann. Surg.*, 1917, lxv, 597) says that one of the earliest effects of sudden and complete obstruction of the ureter is the production of an intense hyperemia and edema of the kidney. The intrarenal pressure slowly rises by damming back the urine which is being formed, and this in turn produces a slow but constant dilatation of the uriniferous tubules. This compresses the venous capillaries, especially those in the cortex, and serves to perpetuate the changes already started. At first only the venous capillaries are affected, but later the artificial circulation also becomes involved. If then the venous apparatus both in the fat capsule and on

the surface of the kidney is well developed, as it usually is, the anastomoses described by Tuffier and Lejars will take up the work for which they were intended and carry on, more or less perfectly, the venous circulation of the kidney. If, on the other hand, as may occasionally happen, this accessory, venous circulation develops either not at all or but slowly, the secretion of urine soon ceases, hydronephrosis will not develop, and atrophy of the kidney will take place. From an experimental study on seven dogs, he concludes that: Sudden, complete and permanent obstruction of one ureter produces hydronephrosis in animals in the vast majority of cases, but atrophy of the kidney may develop in rare cases. When hydronephrosis occurs the venous collaterals of the kidney are well developed; when atrophy of the kidney takes place it is due to a lack of development of these collaterals. Atrophy of the kidney may be produced experimentally, by simultaneous ligature of the ureter and veins which maintain the collateral venous circulation of the kidney. When the obstruction to the ureter is partial or intermittent the hydronephrosis is of greater size than when the obstruction is complete, sudden and permanent, for in the latter event, urinary secretion ceases before the venous collateral circulation has time to develop.

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**Results of Surgical Treatment of Gastric Ulcer.**—Balfour (*Surg., Gynec. and Obst.*, 1917, xxiv, 731) based the following conclusions on 677 gastric ulcers operatively demonstrated in the Mayo Clinic during the past ten years: For ulcers of the pylorus, posterior gastro-enterostomy is the operation of choice in the poor surgical risk, for although pylorectomy is followed by better results, the operative mortality is distinctly higher. The cautery is a useful adjunct in selected cases. For ulcers on the lesser curvature, cautery by the method described in a previous paper and gastro-enterostomy is the operation of choice. Local excision alone of such ulcers is inadequate, 32 per cent. of patients so operated on ultimately requiring further operative treatment, viz., gastro-enterostomy. Sleeve or segmental resection, especially in large, high ulcers and hour-glass contraction in suitable cases is not only a relatively safe operation but has been followed by good results. The lowest operative mortality in the more common operations was associated with cautery and posterior gastro-enterostomy. Ulcers on the posterior wall are associated with the highest operative risk, while those at the pylorus are of least risk.

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**Growth of Free Bone Transplants; An Experimental Study.**—Todyo (*Surg., Gynec. and Obst.*, 1917, xxiv, 701) says that the bone with its periosteum, if it is transplanted in the same body under favorable conditions, continues to live. While among the various components of the transplanted bone the bone cells and the marrow have changed their ability to take the nuclear stain at the end of the third week after the transplantation, the periosteum, the subperiosteal tissue, the epiphyseal cartilage and the epiphyseal line, give distinct evidences of life. Among the various components of the transplanted bone the periosteum and the subperiosteal tissue have not only lived throughout every period of the examination but have executed an active formation of new bone. Most of the epiphyseal cartilage and epiphyseal line have

lived throughout every period of examination, as has the periosteum, and they have, moreover, carried on an active proliferation and ossification. Yet they are irregular, losing their physiological relationships. The bone cells and the marrow have lost or changed the staining power of the neucleus in a short time after the transplantation but the physiological or nearly physiological appearance retufns after a certain time, being replaced by the resistant components of the transplants. The aperiosteal transplant grows and regenerates by the proliferation of cells in the subperiosteal layer. But in each case the new growth of bone is not so active as in the transplants with periosteum. The aperiosteal transplant acquires a new periosteum. The aim of the bone transplantation can be reached without the periosteum and marrow of the recipient. As to the continued life of the transplanted bone, however, Todyo cannot give a definite opinion at this time. Transplanted bone grows; the increase in thickness is marked, although the length increases but little when transplanted with the epiphyseal line.

## THERAPEUTICS

UNDER THE CHARGE OF

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**The Intramuscular versus the Intrathecal Route in the Treatment of Tetanus by Injection of Antitoxin.**—Bruce (*Lancet*, 1917, excii, 680) relates experiments on monkeys undertaken to establish whether the intramuscular or the intrathecal administration of tetanus antitoxin has greater protective forms against tetanus antitoxin. Although the experiments are at present few in number Bruce believes that the results are distinctly in favor of the greater efficacy of the intrathecal as against the intramuscular method.

**A Report of Twenty-five Cases of Tetanus.**—Dean (*Lancet*, 1917, excii, 673) reviews 25 cases of tetanus treated by tetanus antitoxin administered by intravenous, intrathecal, intramuscular and subcutaneous injection. Of 5 mild cases treated by intramuscular and subcutaneous injections of serum, 5 recovered. Of 14 cases treated chiefly by intravenous injections; thirteen recovered. Of 5 cases treated by intraspinal with or without other injections 3 recovered. Dean says if the signs are well localized and not spreading rapidly, intramuscular injections afford an adequate method of treatment. In severe cases, and in those in which signs are generalized, an intravenous injection of 30,000 units under deep chloroform anesthesia should be given. After such injection the further progress of the disease is usually arrested and definite improvement may be expected two to seven days later. The author believes that the essential principle of serum treatment is

to give a very large dose of antitoxin at the earliest possible moment. This object can be most easily attained by the intravenous route. Dean believes that the danger attributed to intravenous injection of tetanus antitoxin has been exaggerated. In 4 cases serum treatment was confined to a single intravenous dose of 30,000 units. In 3 other cases no serum was given subsequent to the intravenous injection. In these 7 cases recovery was as rapid as in 6 other cases in which subsequent injections were given. The serum of patients was shown to contain free antitoxin at various intervals up to thirty-nine days after an intravenous injection of 30,000 units. Dean emphasizes particularly the beneficial effects derived from prophylactic injections of the antitoxin. He believes it probable that almost all, if not all of the 25 cases here reported had received prophylactic injections in France. In 3 of the 25 cases the disease ran an extremely short and mild course. These were the only 3 patients who had received a prophylactic injection after their arrival in England. The author states that if every wounded soldier, irrespective of the size or condition of the wound, was given a prophylactic injection on his arrival in England there would in all probability be a still further reduction in the number and severity of cases of tetanus. One result of prophylactic injection is to prolong enormously the incubation period, with the result that tetanus may occur after the wounds have completely healed. Therefore it is very important to watch carefully for the earliest signs and sypmtoms of the disease.

**The Intravenous Injection of Arsenobenzol in Concentrated Solution.**—Faire and Marsia (*Presse Médicale*, 1917, xxii, 221) say that they have given 3150 injections of neosalvarsan or novarsenobenzol Billon, dissolved in an amount of water never exceeding 2 c.c. They found that novarsenobenzol dissolved very quickly by the addition of the water to the drug contained in the ampoule and gently shaking it until completely dissolved. Neosalvarsan did not dissolve so readily and they advise that care should be taken to distribute the neosalvarsan in a thin layer over the lateral walls of the ampoule by tilting the ampoule and gently rotating it. This simple manipulation prevents the formation of a semisolid mass at the bottom of the ampoule and allows the drug to go easily into solution. Distilled water was usually used to make the solution, but when it was not available, boiled filtered water was used without producing any untoward reaction. The authors state that the concentrated solution is perfectly well borne and they have not observed any vein irritation produced by the injections. Inflammatory induration has occurred due to leakage from the vessel into the surrounding cellular tissues but is not more marked than that occurring from much more dilute solutions. General reactions were usually not observed; in a few instances very mild general reactions followed the injections.

**The Intramuscular or Subcutaneous Injection of Neosalvarsan.**—Harrison, White and Mills (*British Med. Jour.*, 1917, 2940, 569) write concerning the comparative effects obtained by treating two parallel series of cases of syphilis by intravenous injection of salvarsan, including various substitutes for salvarsan, and by the deep subcutaneous or intramuscular injection of neosalvarsan as its substitutes.

The substitutes used by the authors were arsenobenzol, kharsivan and arsenobillon, and it was found by them that these substitutes had practically the same therapeutic effect as salvarsan. The same corresponding results were also obtained by using novarsenobenzol or novarsenobillon in place of neosalvarsan. The authors state that the intramuscular or subcutaneous injection of neosalvarsan and its substitutes was found to be superior in immediate therapeutic effect to that of the intravenous injections of salvarsan and its substitutes. Spirochetes disappear from syphilitic lesions just as rapidly after the first intramuscular as after the first intravenous injection, and the Wassermann reaction is more quickly influenced. The only practical disadvantage is the discomfort at the site of the injection caused by the deep subcutaneous or intramuscular use of neosalvarsan. This can be largely avoided by dissolving the dose of neosalvarsan in 1 c.c. of a 4 per cent. stovaine solution and making the amount up to 2 c.c. by creocamph cream which melts at 15° C. In a footnote the authors state that the creocamph cream was later replaced by camphophenique with equally good results and this has proven to be the most comfortable method of injection up to the present. The general reaction which follows an intramuscular injection is much less than after an intravenous. The authors believe that the tonic effect of such intramuscular injections is much greater than when the remedy is administered intravenously.

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**A Comparison of the Subcutaneous with the Intravenous and Intrathecal Administration of Tetanus Antitoxin in Experimental Tetanus.**—GOLLA (*Lancet*, 1917, cxcii, 686) says that the results obtained by him in animal experiments show the undoubted superiority of the intravenous and intrathecal methods of administering tetanus antitoxin over the subcutaneous. He believes that tetanus antitoxin injected subcutaneously is absorbed too slowly to be available quickly enough to combat the disease.

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**The Treatment of Syphilis of the Central Nervous System.**—HALLER (*Arch. Int. Med.*, 1917, xix, 997) in his article deals with the comparative results obtained in the treatment of cerebrospinal syphilis by mercurialized and salvarsanized serum. He says that a comparison of the efficacy of the two serums in relieving symptoms and in causing objective changes in signs and in the laboratory findings offers more difficulties than are encountered in a comparison of the reactions from treatment. Tables are given in the article showing the comparative effects on the clinical symptoms and laboratory findings. In his conclusions he states that: "The irritating effect in the spinal canal of serum to which mercuric chlorid has been added in the dose of 0.001 gm. is greater than that of 20 c.c. of salvarsanized serum separated from blood drawn thirty minutes after a dose of 0.6 gm. of salvarsan. The average effect on the laboratory findings in the spinal fluid from one dose of mercurialized serum is greater than from one dose of salvarsanized serum. Unpleasant symptoms are more common following intraspinal mercurialized serum than following salvarsanized serum. The greater irritation of the meninges from mercurialized serum prevents as rapid repetition of the dosage as is possible with salvarsanized serum."

Consequently the results at the end of a year of treatment, if each serum were used to the greatest extent consistent with safety, probably would not show such a discrepancy against salvarsanized serum because of the larger number of doses which could be given. He also states that cases of general paresis, meningitis and cerebrospinal syphilis stand intraspinal treatment with mercurialized serum better than do cases of tabes dorsalis. It is particularly in cases of active syphilis of the meninges that the mercurialized serum is useful. Mercurialized serum has an advantage over salvarsanized serum in case of preparation and in its keeping qualities. For these reasons it can be used under clinical conditions in which the use of salvarsanized serum is impossible, or at least very much more difficult. A comparison of the ultimate results obtained with the individual cases in the two groups is impracticable because of the difference in the total amount of treatment which has been given to the two groups, and also because of the small interval of time which has elapsed since treatment was discontinued, or because many of the group treated with mercurialized serum are still under treatment.

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**The Effect of Ingestion of Coffee, Tea and Caffein on the Excretion of Uric Acid in Man.**—MENDEL and WARDELL (*Jour. Am. Med. Assn.*, 1917, lxviii, 1815) found that the addition of a strong coffee infusion to a purin-free diet causes a marked increase in the excretion of uric acid. The addition of Kaffee Hag—a decaffeinated coffee product—to a purin-free diet does not cause any increase in the excretion of uric acid. If, however, caffein is added to the Kaffee Hag the excretion of uric acid is decidedly increased, as in the case of coffee. The effect of adding tea to a purin-free diet is similar to that obtained by adding coffee to the same diet. The increase in excretion of uric acid after adding coffee, tea or caffein to a purin-free diet seems to be proportional to the quantity of caffein ingested. The increase in the amount of uric acid excreted under these conditions is equal to the quantity of uric acid which would be obtained by the demethylation and subsequent oxidation of from 10 to 15 per cent. of the ingested caffein. The results of this series of investigations suggest interesting possibilities for further research. Additional experiments should be performed to determine whether or not the increase of uric acid excretion is always directly proportional to the quantity of caffein ingested. At the same time, the purin-base content of the urine should be determined in order to learn whether the increase in uric acid excretion is due directly to the conversion of caffein itself into uric acid or to an indirect stimulation of purin metabolism. The whole question is further complicated by the presence of tannin derivatives in all the beverages under discussion. Earlier observations of a number of authors indicate that the ingestion of tannic acid and tannin causes a decrease in uric acid excretion. On the other hand, others fail to show any such results. This phase of the problem could be settled by detannated coffee being used in place of a decaffeinated product. Finally, it would doubtless prove interesting to perform similar series of experiments with dogs and rabbits in order to study the effect of caffein ingestion on the excretion of uric acid and of allantoin in species in which uric acid is not the prominent normal end-product of purin metabolism.

# PEDIATRICS

UNDER THE CHARGE OF

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**Enlargement of the Thymus Treated by the Roentgen Ray.**—FRIEDLAENDER (*Am. Jour. Dis. Children*, July, 1917, xiv, No. 1) emphasizes three facts: (1) The condition is much commoner than is ordinarily supposed. (2) The diagnosis can be made definitely by means of simple physical examination and the roentgen ray. (3) In the roentgen ray is possessed a therapeutic agent which, in and of itself, will effect a cure in a majority of cases. As an illustration of the first fact he cites the experience of Dr. J. E. Benjamin, who saw 225 new cases in a year's service at the University of Cincinnati. Congenital syphilis, famial tendency, and association of hypertrophic pyloric stenosis are mentioned as possible etiological factors in this condition in which no definite etiology has been determined. The principal symptoms are dyspnea, suffocative attacks with cyanosis, and stridor. The physical signs are a bulging mass in the jugulum, enlarged area of thymus dulness on percussion, better elicited by using very light percussion. The roentgen ray is of great use in diagnosis if the plates are made with the patient lying squarely. In this series 100 cases were treated with the roentgen ray. Four deaths occurred. The remainder of the cases were either greatly benefited or apparently cured. In the most instances improvement was noticed from twenty-four to forty-eight hours after the first treatment.

**Relation of Mosquitoes and Flies to the Epidemiology of Acute Poliomyelitis.**—NOGUCHI and KUDO (*Jour. Exper. Med.*, July, 1917, xxvi, No. 1), from the Laboratories of the Rockefeller Institute of Medical Research, state that Culex pipiens from sewer waters of Jersey City were raised in water contaminated with poliomyelitic virus. No infection was caused when large numbers of these mosquitoes were allowed to bite monkeys. Full grown Culex pipiens were fed on infected poliomyelitic monkeys during different stages of the disease. These did not transmit the infection when large numbers were allowed to bite normal monkeys. The injection of horse serum into the intrathecal space to cause a previous disturbance of the meninges did not alter the result. The offspring of mosquitoes, which were either raised in the infected tanks or fed on infected monkeys, were found to be entirely harmless when allowed to feed in large quantities on normal monkeys. There was no hereditary transmission of the virus from one generation to another. A filtrate of the emulsion of adult flies and pupæ of the common blue-bottle fly and house fly, which were reared in the laboratory on slices, emulsion, or filtrate of monkey brain containing poliomyelitic virus, showed no trace of the virus. The intracerebral injection of the filtrate produced no poliomyelitic infection in normal monkeys. The authors point out that the experiments of Rosenau and Brues in 1912

were of a different character. They allowed stable flies to feed first on infected monkeys and immediately afterward on a well monkey. Transmission in these test was mechanical and not in the sense of an intermediary host.

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**The Age and Seasonal Incidence and Communicability of Acute Poliomyelitis.**—HERRMAN (*Jour. Am. Med. Assn.*, July 21, 1917, lxix, No. 3) has studied the statistical results of the epidemic of 1916 in New York City. This is the largest epidemic of the disease on record. He shows that the crippling resulting from poliomyelitis is less than from the other communicable diseases and heart disease. A child with a partially paralyzed limb is less handicapped in the struggle for existence than one with defective hearing or a diseased heart. The other communicable diseases are more common and causes more deaths. Susceptibility is more marked in infants and young children. Young infants are less frequently attacked because less exposed to infection. A large proportion of patients under five years of age do not indicate a mild epidemic. The same increase of susceptibility of the central nervous system is seen in the age incidence of tuberculous meningitis. In temperate climates epidemic occur during the summer months, but sporadic cases occur throughout the year. In Scandinavia, epidemics have extended into the winter months. Meteorological conditions do not play the most important role in the spread of the disease. Seasonal changes in the power of the nasopharyngeal mucous membrane to neutralize or inactivate the virus of poliomyelitis may account for the increased susceptibility. Patients who have had poliomyelitis seem to be more susceptible to ordinary nasopharyngeal infections. The susceptibility of children under thirteen years of age to poliomyelitis is much less than to the other communicable diseases of childhood. It is present in only about 2 per cent. The susceptibility is about fifty times as great, to whooping-cough about thirty-five times, and to scarlet fever and to diphtheria about ten times. Children who are susceptible to poliomyelitis are not necessarily more susceptible to the other communicable diseases. There exists a distinct individual predisposition. Because a majority of the susceptible children have immunized by having had the disease or by having been exposed to it, no large epidemic is expected in New York City for some years. A future epidemic could be controlled if we had a method of detecting the 2 per cent. of susceptible children and could immunize them with convalescent serum.

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**Pertussis Vaccine.**—SHAW (*Am. Jour. Obst.*, July, 1917, lxxvi, No. 475) says that "statistics prove that in young children whooping-cough is the most fatal of the group of so-called infectious diseases of childhood. Fully 80 per cent. of the deaths from whooping-cough in New York State during the five year period, 1910 to 1914 were of infants under two years of age and ninety-six of the whooping-cough deaths were children under five years of age. The importance of controlling and preventing a disease which has such a high mortality in early life and such a long and often protracted course, leaving the child debilitated and susceptible to bronchopneumonia, tuberculosis, and diarrheal disease, cannot be too strongly emphasized. The most rational and important step in the control of whooping-cough is the prevention of the

disease itself. The very great importance of the early recognition and prompt reporting to the health authorities of whooping-cough should be realized by the general public and the medical profession. Every case should be regarded as suspicious until its real nature is ascertained, and while in doubt the child should not be allowed to associate with children. Penalties prescribed by the Sanitary Code for failure to report cases of whooping-cough should be enforced just as rigidly as in the case of infantile paralysis, diphtheria, and smallpox. Infected children should be isolated from other children, and in the street should wear a distinguishing mark, such as an arm band with the words 'whooping-cough' in large letters. The sputum and vomitus should be treated in the same manner as in tuberculous affections. The fact that there are 999 alleged 'sure cures' for whooping-cough is proof that we have not yet found a medical remedy of much value. The discovery of the Bordet-Gengou organism has opened the way for a more rational and scientific mode of treatment. Pertussis vaccines are prepared by several commercial houses, by the New York City Department of Health, and in the laboratories of the State Department of Health. Those prepared and recommended by the commercial houses are polyvalent, that is they are mixtures of vaccines, not only containing the Bordet-Gengou bacillus, but containing the influenza bacillus, streptococci, staphylococci, etc. The vaccines prepared by the New York City and State Departments of Health are pure vaccines, standardized by Wright's method from the Bordet-Gengou bacillus. In influenza Dr. Holt has shown that we may find a cough which clinically resembles that of whooping-cough, so that in these cases the pertussis vaccine would have no effect. There is also a probability that there are several types of Bordet-Gengou bacillus. These facts should be borne in mind before condemning the use of vaccines, which prove unsatisfactory in a small series of cases. Graham and Hess report experiences with pertussis vaccines which they believe warrant their further trial. At St. Margaret's House in Albany, 164 children were exposed to whooping-cough in four different epidemics and only 7 per cent. of the number developed the disease. The vaccines administered were from pure cultures prepared by the State Laboratory. In former days when whooping-cough developed in an institution, fully 50 per cent. of the inmates contracted the disease. The value of the vaccines as a prophylactic measure is undeniable, and they should be administered to every child exposed to whooping-cough. The vaccines are harmless, do not produce severe reactions, and there is no danger of anaphylaxis. The dosage used for prophylaxis at St. Margaret's House is the same as the dose for treatment, namely, five hundred million, first injection, one billion for the second, two billion for the third, giving the injections every second or third day. We have administered with good results, one billion every two days for ten days. The results of the vaccines in the treatment of cases already in the paroxysmal stage are not as striking as in prophylaxis, but the concensus of opinion of those who have employed the vaccines, is that where the proper vaccine is used there is a shortening of the paroxysmal stage, with a reduction in the number and severity of the paroxysms. A study of the use of vaccines in 212 cases of whooping-cough, in which this was the only treatment employed, shows that in 38 per cent. of the cases in which the vaccines were given after

the whoop developed, the course of the disease was shorter than the usual duration of the whooping stage, but with no effect on the number or the severity of the paroxysms. In 12 per cent. of the cases there was no improvement either in the course of the disease, its severity or the number of paroxysms."

## OBSTETRICS

UNDER THE CHARGE OF

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**The Bactericidal Property of Vaginal Secretion.**—HARADA has studied this subject at the Obstetrical Department of the Kyoto Imperial University (AM. JOUR. MED. SC., August, 1916). He reviews the literature and describes his own methods of experimentation. He found that all of the vaginal secretion collected during his experiments was acid in reaction and that the bactericidal power of this secretion in pregnant patients increased in potency with the progress of pregnancy, reaching its climax on and after the eighth month. The bactericidal power of this vaginal secretion is strengthened with the increase in acidity. There is no other great difference in the action of this secretion upon various species of bacilli. In some cases the lactic acidity of this secretion was as much as 0.9 per cent., and although the bactericidal power of the secretion increased during pregnancy, the lactic acidity does not. The results of the writer's study show that the bactericidal power is greatly increased by the lactic acid contained in the vaginal secretion, but it was also found that the neutralized vaginal secretion possesses still some bactericidal power. There was reason to believe that certain substances are destroyed at 56° C., which are capable of killing bacteria and other substances that are only destroyed by the removal of the acid. A test was made with chemically pure lactic acid to observe its bactericidal power, and it was found to be far less than that of a vaginal secretion in a ten months' pregnancy. It was further found that although lactic acids are contained in equal quantity in vaginal secretion, the bactericidal power of the vaginal secretion is not unvarying, but increases during the course of pregnancy. There is thus abundant evidence that lactic acid is not the only agent in vaginal secretion in pregnancy capable of destroying bacteria, nor is the bactericidal power of this secretion entirely destroyed by heating to 56° C. The activity of this secretion is considerably lessened by such heating, but is not destroyed. Vaginal secretion during pregnancy may possess considerable amount of dialyzed tissue juice, and it can readily be seen that healthy tissues or blood contain several bactericidal substances. Such are termed by bacteriologists bacteriolysin or amboceptor. If amboceptor is the principal bactericidal substance it is necessary to complete its property with complement. On experiment it was found that the addition of complement fails to render the secretion effective; the bactericidal property of vaginal secretion is not

bacteriolysis, which is necessary to complete its property with complement. Metchnikoff believed that cytase was the active agent in this phenomena, and Gruber-Futaki thought that leukin was the active agent. Cytase is destroyed at 56° C. while leukin is not, and both are thought to be produced by the leukocytes. As leukocytes are abundant in vaginal secretion, it seems reasonable to believe that they have much to do with the bactericidal property of this secretion. It was found that frozen solution possesses stronger bactericidal power than the unfrozen, and on further experiment it was found that the bactericidal substance was partly decreased by heat. From his studies the writer believes that the bactericidal property of pregnant vaginal secretion is not greatly affected by different bacilli. This property gradually increases during the course of pregnancy. Lactic acid in quantity 0.9 per cent. is contained in pregnant vaginal secretion and does not increase during the course of pregnancy. A substance which destroys bacteria in pregnant vaginal secretion is not in the nature of bacteriolysis, which is completed by association with complement. This secretion owes its power to destroy bacteria to the presence of leukin, cytase or allied substances and lactic acid. Leukin is probably an important factor in the bactericidal activity of pregnant vaginal secretion.

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**Role of the Anteposed Uterus in the Causation of Backache and Pelvic Symptoms.**—In examining patients in early pregnancy it is not uncommon to find cases in which the uterus is anteflexed, strongly anteverted and pushing downward, sometimes behind the pubis. Such patients often complain of considerable pain, disability and backache. HUTCHINS (*Jour. Am. Med. Assn.*, September 23, 1916) in these cases, notes the relative position of the cervix to the symphysis pubis and pays no attention whatever to the forward or backward position of the fundus. The amount of posterior descent of the cervix toward the coccyx, and not toward the outlet of the pelvis, was carefully noted. The stability of the lower part of the broad ligament, paracervical tissues and the uterosacral ligaments was tested by grasping the uterus between the examining hands and moving it as far as possible up behind the symphysis and backward toward the coccyx. By this manipulation the backache and dragging feeling of which the patient complained was frequently reproduced. To test the question of treatment, vaginal tampons were so placed that the whole uterus was forced well forward up back of the symphysis in the position where high suspension would hold it. These tampons were allowed to remain for forty-eight hours, the patient moving about freely and if the backache and dragging were relieved, it was believed that suspension would cure. In cases subjected to operation, as soon as the abdomen was opened the intestines were gently pushed up out of the pelvis and a careful exploration of all pelvic structures was made. The uterus was found far down in the pelvis, although there had been no descent toward the outlet. The fulness and congestion of the ovarian veins is very striking in these cases, the chief tension coming on the infundibulopelvic ligament composed of two layers of sensitive parietal peritoneum enclosing the ovarian vessels. This stretches around the side of the pelvic wall originating at a point posteriorly, corresponding

to the location of the sacro-iliac joints. The ovarian veins in this position become engorged up to a point where they cross the pelvic brim, but above that point they were nearly flat and empty. By slowly lifting the fundus out of the pelvis these veins were emptied, the stretched infundibulopelvic ligament relaxed. This explanation of the cause of pain when the uterus is anteposed and carried downward and backward, explains the discomfort of pregnant patients in whom the ovarian veins and all vessels of the broad ligaments are congested. While during pregnancy it would not be advisable to suspend such uteri, if the patient would take the knee-chest posture and practice deep breathing, much relief can be obtained. As pregnancy advances and the uterus unfolds and rises above the pelvis, the symptoms usually disappear.

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**Diagnosis and Management of Extrapelvic Conditions during Pregnancy.**—ANDREWS (*Surg., Gynec. and Obst.*, December, 1916) groups these conditions as (1) injuries and accidents of all kinds; fractures; contusions; wounds, internal and external. (2) Surgical abnormalities, infections, abscesses, and mycoses of various abdominal organs, chest, neck, brain, and extremities. (3) Associated problems of the ductless glands and their metabolism during pregnancy; including the problems of serology and diagnosis as altered or vitiated by pregnancy. (1) In traumatic emergencies during pregnancy there may be an absolute indication for saving the life of the mother. Even in these cases the mode of anesthesia, method of operating, and management of the patient must be modified because of the pregnancy. When pregnant women have fractures, wounds, contusions, or other trauma the surgeon must take care to avoid shock—prolonged anesthesia, and operations which tend to produce uremia. Abortion not infrequently follows prolonged and difficult operations upon pregnant patients. What is absolutely necessary must be done, but as little as possible. (2) Non-traumatic surgical diseases must be treated on general principles. Such are appendicitis, gall-stones, gastric ulcer, tuberculous peritonitis, and allied conditions. As a rule, it is best to do no operation during pregnancy which can properly be postponed unless conditions arise which demand operation in the interests of the mother only. Each case of surgery in pregnant women is to be decided on its own merits. In the puerperal period, general principles again must be the guide of the surgeon. A dislocated kidney may often complicate pregnancy and parturition and prove a grave factor. If discovered early such a kidney may be fixed, although delivery can usually take place without operative interference. It is rarely necessary to operate upon varicose veins in the extremities during pregnancy. (3) In abnormal conditions of the ductless glands the relation existing between the generative organs and these glands must be remembered, and conditions may be found virtually caused by the pregnancy which would not otherwise be present from disease of the ductless glands only. The writer calls attentions to the danger of the use of salvarsan in pregnant women unless the arsenic which it contains is freely excreted. He adopts the rules laid down by Raeder that women expecting to be pregnant should be given a thorough physical examination. Every functional defect should be corrected before pregnancy. No operation should be per-

formed during pregnancy if it can be deferred, but any operation which will contribute to the safety of the patient should be performed although the patient be pregnant.

**The Diagnosis and Management of Pregnancy in the Presence of Acute Abdominal Conditions.**—DeLee (*Surg., Gynec. and Obst.*, December, 1916) draws attention to the confusion which frequently arises between ectopic pregnancy and appendicitis. The rising leukocyte count, taken every two hours, is essential in making a diagnosis. When ectopic gestation and pregnancy coexist, or ectopic gestation and salpingitis, the diagnosis may be difficult. It is necessary to make a careful vaginal examination in these cases, or otherwise pregnancy may not be suspected and pernicious nausea of pregnancy may prove fatal because confused with obstruction of the bowel. A case is described in which a woman had a gestation in the left tube, the fetus escaping into the abdomen, while the pain and rigidity, jaundice, nausea, and vomiting pointed to the gall-bladder. Ectopic gestation, so soon as a diagnosis is made, should be treated by abdominal section. Appendicitis may be confused with pyo-ureteritis and also colon bacillus infection, not uncommonly seen in pregnant women. In these cases the patients have symptoms of ureteritis, appendicitis and cholecystitis, the colon bacillus being found in the urine. In some cases jaundice develops. Acute appendicitis in pregnancy demands immediate operation, disturbing the uterus as little as possible. Should abortion be threatened at the time of operation, the uterus should first be emptied and then the abdomen opened. If the woman is at term, Cesarean section should be avoided, but the appendix should be dealt with and opium be given to prevent labor. Should the operator find that general peritonitis is present, it would be better to do hysterectomy, draining the pelvis from below. Pyosalpinx should be dealt with by removal, but cholecystitis, as a rule, does not require operation during pregnancy. In the presence of ileus, abdominal section is safest. In pyelitis, Cesarean section is not indicated for fear of infecting the birth canal. The kidney may be drained, if necessary. Uterine rupture demands section, and injury to the abdominal contents, especially the uterus, calls for immediate operation. Hernia and ruptures of various sorts are best treated by operation. In general, it is better to postpone operations on pregnant patients until after delivery.

**Diagnosis and Management of Pelvic Infections Complicating Pregnancy.**—Lewis (*Surg., Gynec. and Obst.*, December, 1916) believes that retroversion of the uterus during pregnancy is a grave condition, frequently resulting in abortion. When adhesions are present it may be safer to open the abdomen, separate the adhesions, and replace the dislocated uterus. Suspensory operations should be avoided during pregnancy. When pregnancy has gone beyond the fourth month it is generally safest to empty the uterus by abdominal section and to relieve the patient before symptoms connected with the bladder can develop. All cases of rupture of the uterus should be dealt with by section, but the management of the case after the abdomen is opened will depend upon the extent and location of the rupture, the amount of hemorrhage, chances of infection and somewhat on the age of the patient. When the rent in the uterus is clean cut, it is occasionally

possible to suture the uterine muscle and retain the uterus; ordinarily supravaginal amputation is indicated. Acute salpingitis in pregnancy does not demand surgical treatment. Tubal abscess, or other pelvic collections of pus should be opened through the vagina, especially during the early months of gestation. It is often impossible to distinguish between pelvic abscess and ectopic pregnancy, and frequently on opening the pelvis to empty an abscess an ectopic pregnancy is found. Ovarian tumors complicating pregnancy should be removed so soon as possible. The writer thinks that after the fifth month the uterus is so high in the abdomen and is obstructing the entrance to the pelvis so completely that removal of an ovarian tumor from the pelvis would be attended with great difficulty. The frequency of torsion of the pedicle must be remembered in these cases, which is an added reason for the early removal of the tumor.

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**Rupture of the Uterus, Sepsis, Operation and Recovery.**—HALL (*Am. Jour. Obst.*, December, 1916) reports the case of a multipara, who had a quick and unaided labor, and, on the fourth day, a chill and temperature, which rose rapidly to 104° F. An afternoon rise and a normal morning temperature continued for some time, the patient feeling well except for slight pain or tenderness in the right lower half of the abdomen. The lochia seemed normal. The patient had no chills or sweats, good appetite and felt well, and had abundant nourishment for the child. Five weeks and three days after labor, the patient had a severe chill, the abdomen was moderately distended, not sensitive to palpation, except in the right lower quadrant; muscular rigidity was moderate on that side. No mass could be felt in the abdomen or pelvis except a large, subinvoluted uterus. Bimanual examination revealed that involution was going on well. The most natural inference was that the patient had a small ovarian cyst which had ruptured during labor. No interference at first was practised, and the patient continued to do fairly well. The temperature, however, continued to rise, and tenderness and rigidity in the right half of the abdomen were more marked than before. Six weeks after delivery the patient was growing worse. She had profuse sweats, the mass in the abdomen appeared to be three times the size it was four days previously, and more sensitive. She seemed septic, although able to nurse her child. On operation, the omentum was found adherent, and, on separating the adhesions, pus was found in front and to the right of the uterus. There had been a rupture of the uterus at the fundus, extending down to the top of the bladder. In this rent the omentum had inserted itself and was firmly adherent. The uterus was larger on one side than on the other. The omentum was severed close to the uterus and all that portion in contact with the pus-cavity removed. The appendix and Fallopian tube on that side were not involved. It was found that the ruptured surfaces in the uterus had healed spontaneously and hence the uterus was not molested. In discussion, Schwartz described a case in whom an effort was made to induce labor for contracted pelvis. Labor developed, but suddenly the uterine contractions ceased and the patient became absolutely quiet. The child was immediately extracted by the feet, and as soon as possible the abdomen was opened and a rent in the uterus repaired. A second case was that of placenta previa in which a general practitioner had applied a pack and then given ergot. The result was strong uterine contractions followed by rupture.

# PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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**Transplantation of Benign Tumors.**—In a detailed report on the transplantation of benign tumors in which six rat tumors were employed, LOEB and FLEISCHER (*Jour. Cancer Research*, 1916, i, 427) give the results of some extended experiments. The transplants were carried to the second and third generations whenever possible. Both auto- and homoiotransplantation were employed in each tumor studied. The writers, at the outset, found themselves facing difficulties which they resolved into three general questions. These may well be stated, and, with each the data resulting from their work. Primarily, their previous experience in the study of cancer led to a comparison between the growth of this tumor and the benign forms, under experimental conditions. They demonstrated that, like the malignant tumors, the benign forms can be transplanted through several generations, during which process they show both gross increase in size and microscopic evidence of proliferation. While this is true they also found that though malignant tumors increase in growth energy, possibly directly due to stimulation of tumor cells by the conditions of transplantation, benign tumors decrease in growth energy. This is apparent in the greater latent period seen in each generation of transplants over that preceding, as well as in the microscopic evidence of definitely slower proliferation. The benign tumors, whether because they are less embryonal, or contain more fibrous tissue, or are better able to vascularize themselves, have been found to be more resistant to transplantation. Also, the growth is frequently better in case a benign breast tumor is transplanted into a pregnant animal. Malignant tumors as well as embryonal tissues are found to be difficult or impossible to transplant into animals in pregnant state. This then brings up the second question, How does the growth of benign tumors compare with that of normal tissues? Craster has demonstrated that transplanted skin soon regains its equilibrium and does not undergo progressive growth. Later transplants were found to grow better than early ones, suggesting that the mere operative trauma incident to removal of the tissue for transplantation had in some way stimulated growth energy. In regard to the increased growth manifested in benign breast tumor transplants with the occurrence of pregnancy, the authors are convinced that this phenomenon is due to a specificity in reaction of this tissue similar

to that seen in the normal breast under like influences, and due to a definite chemical constitution of the tumor tissue. It is admitted, however, that in one instance the best growth in the second generation was obtained in a male rat. This almost seems to destroy the only theory offered, and rather to suggest simply the influence of chance in the growth of transplants. Lastly, to the question whether it is easier to bring about by experimental means the transformation of a benign into a malignant tumor than to effect a similar transformation of normal tissue, little can be given. The author suggests that growth energy in benign tumors should be studied with the aim of producing an increase in this quality. Up to the present, the decreased growth energy demonstrated in the transplantation of these tumors gives little encouragement to the prospect of inducing malignant change in benign tumors.

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**The Inheritability of Spontaneous Tumors of Specific Organs and of Specific Types in Mice.**—During the past few years, much valuable work has been completed on experimental tumor growth. Mice have been most widely used in this type of study. As a result, certain definite postulates have been established, notably by Slye, who has maintained a large colony of mice of various strains under ideal hygienic conditions for a period extending over ten years. This has facilitated a careful study of the heredity of the animals used and has also produced a rugged stock, capable of living well over the tumor-bearing age. Following these strains, it has been possible to show that tumor development has a persistent tendency to recur in strains where it has been introduced by breeding. This persistence withstands both inbreeding and hybridization. Other strains, non-cancerous, have never developed tumor, either by inbreeding or by hybridization with proved non-cancerous strains. Cancer can be introduced into non-cancerous strains, however, by hybridization with cancerous individuals, and from such crosses it is possible to obtain strains which never produce cancer as well as strains which always do, and which carry it into any strain with which they may be hybridized. Hence, the behavior of mouse cancer in heredity is similar to that of a Mendelian recessive characteristic. Slye (*Jour. Cancer Res.*, 1916, i, 479) now reports some concrete instances of heredity. In a strain of Japanese white-footed mice, which has presented many tumors of all types in addition to the commoner ones of breast and lung, there gradually developed a period of remission in which tumors became rarer, and there were very few of the unusual varieties. As the hybrids of this race began to attain the cancer age, the incidence of tumors of all sorts again became high. As an example primary ovarian tumors may be mentioned. Out of the first 2200 autopsies, there were eight primary ovarian tumors; in the next 4000 no ovarian tumors; and in the last 3000 six primary ovarian tumors. The same is true of liver tumors, where more than half of the whole number obtained has been found in hybrids of the original tumor-bearing strain, only now coming to the tumor-bearing age. The author emphasizes in her report that the inheritability of these tumors is strongly brought out by the fact that while this strain has been subject to exactly the same environment as the others of her stock, nearly all the unusual forms of tumor have come from this one strain. Uterine

tumors, also found in this strain, were a further interesting and striking instance of inheritance of a tumor of specific type in a specific organ. A female, inbred with her brother, gave rise to a strain producing 3 out of the 4 uterine tumors found in the entire group of animals studied in the first 2000 autopsies. Outbred with a male of another group, she obtained a strain producing the only other uterine tumor of the same series of autopsies, and in addition, her direct descendants by both inbreeding and hybridization, headed families producing further uterine tumors. A suggestion substantiating trauma as an etiological factor is given in connection with a curious fibromatous growth, infiltrative in character, which appears on the back and sides, following repeated light scratches, severe enough to result in scarring. An area of baldness develops, followed by an induration which becomes deeper rather than wider. Finally the entire posterior portion of the body undergoes a stiffening, and death results from inability to move to food and water. This form of tumor is inheritable, and has been followed through two successive generations. The author thus claims that tumors of specific organs and specific types are inheritable, and that by selective breeding it is possible to develop a higher percentage of any type of tumor, which may then be carried into another line, free of tumor, and run true to form in the offspring. In another paper (*Jour. Cancer Res.*, 1916, i, 503) the author develops this theme further, in a study of the inheritability of spontaneous tumors of the liver in mice. This type was selected as one which would offer substantial evidence on the influence of inheritance on tumor development as this tumor is not so frequently found as those in the lung and breast, nor is it so rare as to be questioned, as might be the case with tumors of the uterus and stomach. All the liver tumors, including 62 primary and 17 secondary liver tumors, have come from one strain and the animals showing this type of new growth all have an identical ancestry. A few examples will serve to illustrate the manner in which the details have been worked out. A male having an adenoma of the liver, mated to a female with liver tumor, gave a family in which there was a high percentage of liver tumors. The same animal, mated to a female without liver tumor showed no liver tumor in the offspring, though the percentage of tumor in this family was high. Another strain, especially selected to show the inheritability of liver tumor, was sired by a male with a malignant adenoma of the liver. The male offspring constantly showed tumor, though always bred to a female without tumor, and not of the direct line. In the fifth and sixth generation, primary liver tumors again appeared. The data presented appear convincing, especially since outside of the author's stock, but one instance of liver tumor has been reported and in view of the fact that in attaining these results selective breeding has been the only manipulation employed.

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**On the Etiology of Scarlet Fever.**—The infecting agent of scarlet fever still baffles the investigator. Periodically researches are undertaken in an attempt to determine the infecting microörganism and often some bacterium is found, which, though satisfying the investigator in his studies, has proved disappointing to others in failing to fulfil the requirements proving it the causative factor of scarlet fever. During 1916 two new microörganisms were offered by independent

workers as the etiological factor of scarlet fever. MAIR (*Jour. Path. and Bact.*, 1916, xx, 366) isolated from the throats of scarlet fever patients a micrococcus which he called the Diplococcus scarlatinæ and which on cultivation showed itself to be related either to the pneumococcus group or to the group of streptococcus viridans. Mair himself believed that the relation with the pneumococcus was quite close, although capsules as a rule could not be demonstrated. The microorganism produced green colonies on blood agar, caused milk to clot and become acid, and fermented many of the carbohydrates including lactose, salicin and inulin. Mannite was fermented by some strains but not by all. The microörganism dissolved in bile, a characteristic which is distinctive of the pneumococcus. A low pathogenicity was demonstrated for mice and rats while rabbits showed a greater susceptibility. Guinea-pigs were fairly refractile. The author claimed to have obtained peculiar reactions in the monkey associated with fever, Doehle's bodies in the leukocytes and a spreading inflammation beneath the skin. Local sloughing or abscess formation ending in recovery or toxemic death in the second, third or fourth week in treated monkeys, was regarded as typical by the author for the Diplococcus scarlatinæ. Control experiments, using typical pneumococci from other sources, gave no such reactions. A certain grade of immunity was conferred upon infected monkeys which recovered. The author was able to isolate the microörganism from the throat of 42 patients out of a total of 50; while, in a control series of 35 cases, no organisms corresponding to the Diplococcus scarlatinæ were found, although from 12 of them typical pneumococci were obtained. In concluding upon the specific nature of the Doplococcus scarlatinæ, the author placed weight upon the finding of this microörganism in 80 per cent. of the cases, the reproduction in the monkey of "a disease which in many respects resembles scarlet fever," and the development in the monkey of "scarlatinal rheumatism." The rash of scarlet fever has not been observed in animals. Almost simultaneously with the report by Mair, a preliminary note upon the same subject was issued by MALLORY and MEDLAR (*Jour. Med. Res.*, 1916, xxxiv, 127) and was subsequently followed by a more extensive paper (*Jour. Med. Res.*, 1916, xxxv, 209). These studies were mainly of a histological kind, wherein tissues obtained at autopsy from cases of scarlet fever were analyzed. These studies were supplemented by cultural methods upon about 60 patients. The authors found a Gram-positive bacillus (B. scarlatinæ) which is usually less virulent than the diphtheria bacillus but which, as a rule, affects the the same localities, the tonsils and pharynx, and in severe cases may extend to the adjoining tissues. The organism is held responsible for the necrosis of the lining epithelium and the exudation of serum and leucocytes occurring in the deeper structures. In uncomplicated scarlet fever the bacilli were found in large numbers in lesions in the respiratory tract, from which, however, they rapidly disappeared following the appearance of the eruption. Occasionally the microörganisms were found for longer periods of time. On three occasions a similar bacillus was found in stained sections of postmortem material, while cultures of a similar microörganism were obtained in five instances at autopsy. The bacillus was smaller than that of diphtheria but appeared to belong to the same group of microörganisms. In a few instances

serum from scarlet fever patients gave a positive complement-fixation test. Animal experiments using monkeys, rabbits, guinea-pigs, rats and mice gave inclusive results.

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**War Nephritis.**—The present war has demonstrated many new phases in the development of disease as well as brought to light a number of conditions previously unknown to medical literature. The very character of the warfare on land has placed the individuals of the armies under conditions which have heretofore been entirely unknown to civil and military life. The trenches, although not new, have been developed upon such a scale that the soldier makes his home day and night in these constructions, which at different seasons in the year place him under conditions, particularly in exposure to wet and cold, to which he has been unaccustomed. Furthermore, the enormity of the armies gathered upon the field of war is so tremendous that the hygienic handling is one of great difficulty. There are, therefore, many circumstances which may influence the spread of infection and the development of disease. RUDOLPH (*Canadian Med. Assn. Jour.*, 1917, vii, 289) in a recent communication discusses the occurrence of war nephritis or what others have presumed to call "trench nephritis." This disease is not entirely new, as it was observed in the Civil War. The author had an opportunity of seeing about 200 cases of this condition. Its development in the army occurs almost in epidemic form so that in certain seasons numerous men seek the hospital for renal disturbances. Rudolph points out that the term trench nephritis is a misnomer for it is unnecessary to have lived in the trenches to suffer the affection. In the majority of instances the individuals had previously been robust and without an ailment. A few had had an antecedent sore throat or bronchitis. Edema was an early manifestation and was commonly the condition which warned the individual of his trouble. Headache was not uncommon and nocturnal dyspnea occurred in 78 per cent. A rise in blood-pressure was noted in about one-half of the cases studied. In a number of instances the nephritis was a recurrent one, the individual giving a history of previous illness having no relation to the military conditions. The cases which were clearly primary varied from mild to very acute attacks showing coma and convulsions. In the series reported 6 per cent. had convulsions. Only one case died and this was a recurrent one with small granular kidneys. The author believes that the condition has its basis in infection and is of the nature of a glomerulonephritis.

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**The Pathological Effects of Streptococcus from Cases of Poliomyelitis and Other Sources.**—BULL (*Jour. Exper. Med.*, 1917, xxv, 557) inoculated guinea-pigs, cats, dogs, rabbits and monkeys with cultures from the tonsils of 32 cases of poliomyelitis; carrying on, in other words, the same experiments as Mathers, Herzog, Nuzum and Rosenow. His results were widely different from those of these previous authors who claim to have produced poliomyelitis clinically and pathologically by the inoculation of streptococci into the same laboratory animals. In no case was the author able to induce conditions resembling poliomyelitis either clinically or pathologically. A considerable percentage of rabbits and a similar percentage of some of the other animals developed lesions

due to streptococcus, such as meningitis, arthritis, endocarditis, abscesses of kidney or brain, etc. Seventy-eight rabbits received intravenous injections of cultures from poliomyelitis patients; 76, cultures from non-poliomyelitic sources. The distribution, character and frequency of the lesions were the same in both series. Moreover, conditions and lesions were produced in rabbits not found in man or the monkey. The author was also unable to detect any immunological relationship between the streptococcus and the filterable virus of poliomyelitis. Monkeys immunized against streptococci developed poliomyelitis when inoculated with the filterable virus. Streptococci isolated from the poliomyelitic brain and spinal cord of monkeys which had succumbed to inoculation with filtered virus failed to induce in other monkeys any paralysis or change characteristic of poliomyelitis.

## HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

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**Cultivation Experiments with the Blood and Spinal Fluid of Pellagrins.**—FRANCIS (*Hyg. Lab. Bull.*, No. 106) carried out anaërobic cultivation on the blood and spinal fluid of pellagrins, somewhat after the method described by Noguchi for growing spirochetes. Blood and spinal fluid were cultured from each of 17 colored pellagrins at the State Insane Asylum, Milledgeville, Georgia, 7 of which proved fatal between six and thirty-seven days after the materials were obtained from them. In addition, blood was cultured from 4 mild cases at the U. S. Marine Hospital, Savannah, Georgia. Each inoculated culture tube contained (*a*) fresh rabbit kidney; (*b*) either ascitic fluid or a mixture of 1 part ascitic fluid and 2 parts meat-infusion agar (+0.5), which latter, in some cases, contained 2 per cent. of glucose; (*c*) either fresh spinal fluid drawn by lumbar puncture or fresh blood drawn from the median basilic vein (defibrinated or citrated); (*d*) either a 1-inch column of sterile paraffin oil or no oil. All culture tubes were incubated without the use of special anaërobic apparatus at 37° C. for two or three weeks, at the end of which time examinations were made with the dark-field microscope. The method of cultivation employed furnished conditions of growth suitable for strict anaërobes, strict aërobes, and for facultative organisms of either group. Anaërobic conditions were most nearly approached around the kidney tissue at the bottom of the oil-covered tubes. To a less degree there

was anaërobiosis at the bottom of the uncovered tubes. Conditions for aërobic growth were found on the surface of those tubes of the media which were not covered with oil. There were thus studied eight culture tubes inoculated with 10 c.c. of blood drawn from each of 21 cases and eight culture tubes inoculated with 10 to 20 c.c. of spinal fluid drawn from each of 16 cases, making a total of 296 tubes examined. The results of the examination of the cultures were negative; the cultures either remained sterile, or an occasional tube showed a growth which was evidently a contamination.

**The Transmissibility of Pellagra.** — GOLDBERGER (*Public Health Reports*, November 17, 1916, xxxi, No. 46) subjected sixteen volunteers to experiment. With one exception all were men and varied in age from twenty-six to forty-two years. No restraints were imposed on their customary habits or activities. Seventeen cases of pellagra of various types and of different grades of severity furnished some one or more of the experimental materials. The materials were blood, nasopharyngeal secretions, epidermal scales from pellagrous lesions, urine and feces. Blood was furnished by 4 of the cases, nasopharyngeal secretions by 4, epidermal scales by 5, and urine or feces by 16, of whom 10 furnished both urine and feces, 3 urine without feces, and 3 feces without urine. Blood was administered by intramuscular or subcutaneous injection; secretions by application to the mucosa of the nose and nasopharynx; scales and excreta by mouth. Both urine and feces were ingested by 15 of the volunteers, 5 of whom also took blood, secretions, and scale. The experiments were performed at four widely separated localities (Washington, D. C.; Columbia, S. C.; Spartanburg, S. C.; and New Orleans, La.) at which different groups of the volunteers were assembled. Observation has been maintained by association with a majority of the volunteers and by visits of inspection, supplemented by reports from the volunteers themselves, 13 of whom are physicians, and by reports from other medical officers of the service with whom they are associated. During a period of between five and seven months none has developed evidence justifying a diagnosis of pellagra. These experiments furnish no support for the view that pellagra is a communicable disease; they materially strengthen the conclusion that it is a disease essentially of dietary origin, brought about by a faulty, probably "deficient" diet.

**The Effect of Cold upon Malaria Parasites in the Mosquito Host.** — KING (*Jour. Exper. Med.*, March 1, 1917, xxv, No. 3) reports experiments showing that the parasite of tertian malaria in the mosquito host is able to survive exposure to a temperature of 30° F. for a period of two days, 31° F. for four days, and a mean temperature of 46° F. for seventeen days. In a smaller series of tests the sporonts of the estivo-autumnal parasite have shown a resistance to temperature as low as 35° F. for twenty-four hours.

**The Application of the Statistical Method to Public Health Research.** — DUBLIN (*Am. Jour. Public Health*, vii, No. 1) discusses the commoner fallacies and errors that arise in statistical investigations in the field of public health and hygiene. He divides statistical investigations into three stages: (1) Defining the scope of the inquiry, planning

the inquiry schedule, and collecting the data; (2) editing, classifying and tabulating the data; and (3) analyzing and interpreting the results. He points out with many illustrations the fallacies and errors that arise at each stage. In the first stage of public health investigations, the author thinks, errors often result from poorly devised questionnaires and from the incomplete registration of facts. In the second stage, he emphasizes the importance of properly editing the schedules before tabulation and of returning defective schedules to the original source of correction. The use of standard systems of classification is emphasized and errors that result from indifference to the use of standard systems are considered. The gravest errors in the use of the statistical method in public health work, the writer says, arise in the third stage of inquiry, *i. e.*, in the interpretation and analysis of the results. The investigator should make every effort to avoid errors of this kind because it is in this part of the inquiry that the public is most interested. Among the commoner fallacies of analysis are those which arise from the comparisons of statistics that are essentially incomparable, from a confused idea that "proportions" are somehow equivalent to "rates," from the drawing of conclusions from too few cases and the like. In conclusion, he points out the necessity for extreme caution in the collection, preparation, and interpretation of data in public health work. This is necessary if the general public is to be expected to support health movements based on the results of such investigations. Health officers will find in this paper many practical suggestions, that will help them in the research side of their work.

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**Pertussis Vaccine.**—PAUL LUTTINGER (*Jour. Am. Med. Assn.*, May 19, 1917, lxviii, No. 20, 1461) gives a summary of the results of the whooping-cough clinic of the Department of Health of the City of New York. The work was carried out under the supervision of Dr. William H. Park, and the conclusions reached are that the results obtained at the clinic, and also by over 180 private physicians and health officers would warrant the routine administration of pertussis vaccine for both curative and prophylactic purposes. The best time to institute the vaccine treatment, except as a prophylactic, is the first and second week of the paroxysmal stage. When the proper vaccine is given and the method of the department is employed, the disease is materially reduced in duration and severity. The presence of subconjunctival hemorrhages in prophylactic cases which were protected by the vaccine seems to point to its specific immunizing action against the paroxysms and to the fallacy of the hitherto accepted theory that these hemorrhages are due to the violence of the cough.

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**The Possibility of Typhoid Infection through Vegetables.**—MELICK (*Jour. Infect. Dis.*, July 1, 1917, p. 28) reports that the longevity of B. typhosus in soils has shown considerable variations under like conditions in the open. The old strains (1 and 3) survived in garden soils fifty and fifty-three days, while the viability of fresh cultures (strains 4 and 5) was thirty-two and forty-three days, respectively. In sandy soil the longevity of strain 3 was thirty-six days; that of strain 4, twenty-nine days. In three outdoor experiments, extending from May to September, B. typhosus was isolated from garden soil inoculated

with typhoid excreta after forty-one, thirty-four and thirty-five days. Under hot-house conditions in sandy soil, strain 1 survived fifty-three days. The longevity was increased under the same conditions in garden soil enriched with sterile sewage and broth to seventy-four days. Similarly, the viability of fresh culture of strain 2 in garden soil was forty-nine days. No evidence has been found that would indicate the entrance of B. typhosus into the interior of the plants. The organisms become attached to the surfaces from their contact with the soil and are not removed by ordinary washing. Under natural conditions, radishes grown in contaminated soil were found to be still infected with typhoid bacilli in 3 experiments after periods of thirty-seven, twenty-eight and thirty-five days, respectively; and from lettuce, after twenty-one days. This is ample time for the maturing of such vegetables. It may be reasonably concluded that vegetables grown in soil fertilized with fresh typhoid excreta shortly before planting or during the growing season are likely to be contaminated at the time they reach the consumer. Vegetables so contaminated are not made safe by the ordinary method used in the preparation of such foods for table use, and may, therefore, be a source of typhoid infection.

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**The Focal Pulmonary Tuberculosis of Children and Adults.**—OPIE (*Jour. Exper. Med.*, June, 1917) examined fifty adults and found evidence of tuberculosis infection in all of them. Approximately one-half of all adults have encapsulated lesions of the lungs or bronchial lymphatic nodes, whereas in one-third pulmonary and lymphatic lesions are firmly calcified and completely healed. Tuberculosis pulmonary lesions of adults who have died of diseases other than tuberculosis are of two types: (1) apicaltuberculosis similar to the usual type of fatal phthisis and unaccompanied by caseation of the regional lymphatic nodes; (2) focal tuberculosis not more commonly situated in the apices of the lungs than elsewhere and accompanied by caseation (or calcification) of the adjacent lymphatic nodes. Focal pulmonary tuberculosis of adults is identical with the tuberculosis of childhood. It occurs in at least 92 per cent. of all adults. It may be acquired between the ages of two and ten years but in more than half of all individuals (in St. Louis) makes its appearance between the ages of ten and eighteen years. Tuberculosis of children does not select the apices of the lungs, is accompanied by massive tuberculosis of regional lymphatic nodes, and exhibits the characters of tuberculosis in a freshly infected animal, whereas tuberculosis which occurs in the pulmonary apices of adults has the characters of a second infection. Almost all human beings are spontaneously "vaccinated" with tuberculosis before they reach adult life.

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**Methods for the Determination of Pneumococcus Types.**—BLAKE (*Jour. Exp. Med.*, July 1, 1917, p. 67) states that the determination of pneumococcus types in lobar pneumonia is of value in the field of prognosis and as a prerequisite for specific serum therapy. The method for the determination of types should be as rapid as possible and a standard technic should be employed. The most satisfactory method is by the intraperitoneal inoculation of a mouse with the patient's sputum, by which means a rapid and abundant growth of the pneumococcus is

obtained and secondary organisms are rapidly eliminated in most instances. The diagnosis of type is made directly on the peritoneal exudate. Certain factors in the method commonly used have interfered with the rapid determination of types in an appreciable number of cases, notably the growth of other organisms in the peritoneal exudate together with the pneumococcus, and some confusion has arisen because occasional strains of pneumococci have been encountered that show cross agglutination reactions when undiluted immune serum is used. Such reactions have been shown to be due to a limited zone of non-specific immunity and they in no way invalidate the classification of the pneumococci into sharply defined immunological groups. The optimum dilutions of serum have been determined that will agglutinate all type trains of pneumococci and fail to cause any cross-agglutination reactions when mixed with equal amounts of pneumococcus cultures and incubated for one hour at 37° C. They are a 1 to 20 dilution of serum I, a 1 to 20 dilution of serum II, and a 1 to 5 dilution of serum III. For the diagnosis of subgroup II pneumococci undiluted type II serum is required. To obviate the other difficulties of the method commonly used a new method for the determination of types has been devised. It depends upon the fact that there is produced by the growth of the pneumococcus a soluble substance which is present in the peritoneal exudate of the mouse in sufficient quantity to give a specific precipitin reaction with the homologous immune serum. The precipitin method can be used in all instances in which the determination of types by the agglutination method is possible, and it possesses certain distinct advantages which make it available when the agglutination method is impracticable. It is of particular value as a time-saving device in those instances where the presence of other organisms together with the pneumococcus in the peritoneal exudate causes a delay of eighteen hours or more before the type of pneumococcus can be definitely established. It is therefore recommended as the method of choice in all cases. If desired, both the agglutination and precipitin methods may be applied to the same specimen of peritoneal washings.

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**Rocky Mountain Spotted Fever in California.**—KELLY (*Public Health Reports*, vol. xxxi, No. 40) as a result of an investigation of Rocky Mountain spotted fever in Modoc and Lassen Counties, California, reaches the following conclusions: (1) Rocky Mountain spotted fever has existed in California for a much longer period and to a far greater extent than has hitherto been supposed. (2) There are probably five main infected areas, one in Modoc County and four in Lassen. (3) The disease is not as severe in California as in Montana, nor as light as in Idaho. (4) The infection probably entered California through Nevada rather than Oregon.

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Contributions from abroad written in a foreign language, if on examination they are found desirable for this JOURNAL, will be translated at its expense.

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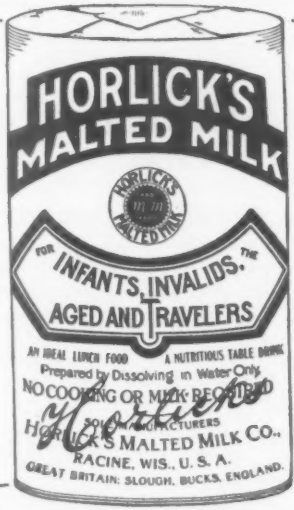
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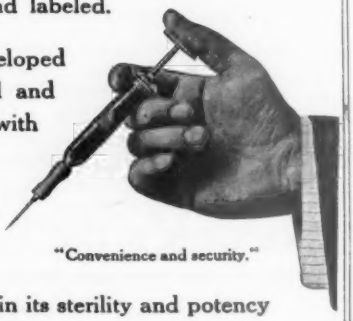

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*See page 443 for Review* **BRITISH MEDICAL JOURNAL, March 10, 1917**

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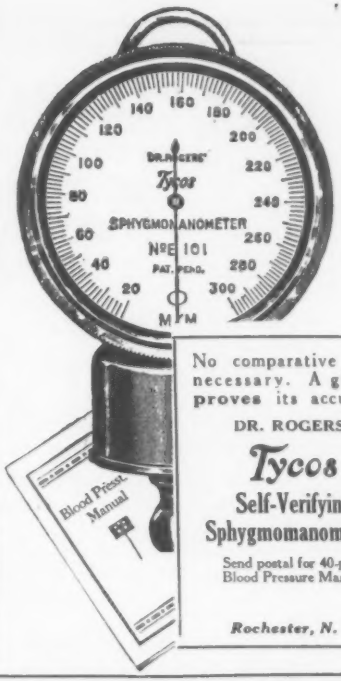


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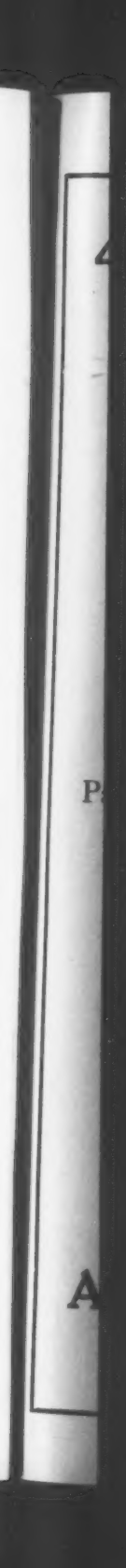

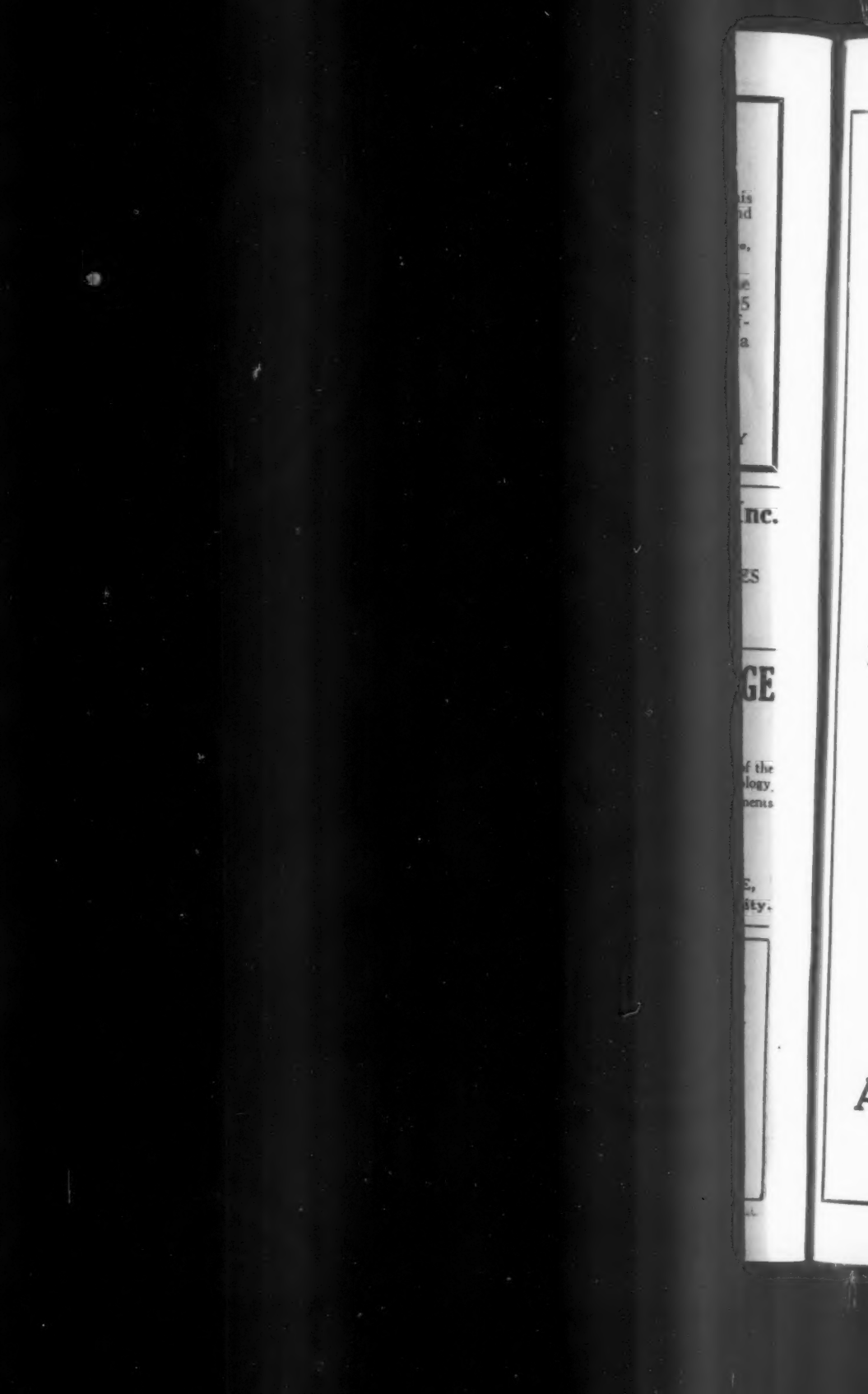

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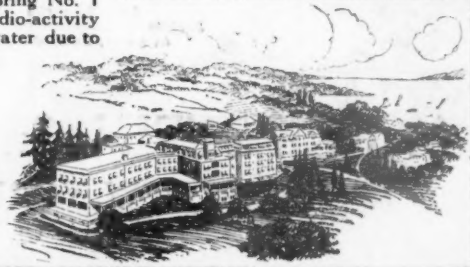
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